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DIAGNOSIS

INDICES to Vol 11 (1971)

January March May July September November

## Contents of Volume 11 — DIAGNOSIS

|  |     |
|--|-----|
| Electric potentials in pulmonary lesions — A preliminary report<br>By B NORDENSTROM  | 1   |
| Intraperitoneal contrast extravasation in lymphography<br>By P E ANDERSEN  | 17  |
| Defects in the urographic contrast medium above and below a ureteric calculus<br>By Ö ARNALDSSON and D HOLMLUND  | 26  |
| Repeat direct pyelography via needle nephrostomy<br>By R VELA NAVARRETE  | 33  |
| Arteriovenous fistulae following percutaneous renal biopsy<br>By L EKLUND and T LINDBOLM   | 38  |
| Angiography in juxtacortical osteosarcomas — Case report with special reference to the differential diagnosis<br>By F P PROBST   | 49  |
| Effects of salicylates on the gastric mucosa as revealed by roentgen examination and the gastroscope<br>By D EDMAR   | 57  |
| The adrenal glands after epinephrophlebography<br>By C G MIKAPLSSON  | 65  |
| Arteriography in arterial gunshot wounds<br>By J GIRL  | 78  |
| Excretion of sodium metrizoate through the liver during urography<br>By O OLSSON   | 85  |
| Relations between the cervical spine and the vertebral arteries<br>By P CONSTANTIN and C LUCRETIA  | 91  |
| Skeletal and tooth development — A methodologic investigation<br>By B LILIEQUIST and M LUNDBERG  | 97  |
| Percutaneous biopsy of vertebrae and ribs<br>By B NORDENSTROM  | 113 |
| Increased biliary concentration of contrast media by combined oral and intravenous administration<br>By M HAVFRLING, J SWEDENBORG and L THULIN                         | 122 |
| Ioglycamide (Bilivistan) as a contrast medium for intravenous cholangiography — A clinical and experimental investigation<br>By J BRISMAR, P LINDGREN and G F SALTZMAN | 129 |
| Phlebography in acute deep venous thrombosis of the lower extremity — A comparison between centripetal ascending and descending phlebography<br>By U BERGVAL           | 148 |
| Angiography in renal tuberculosis<br>By R BJORN HANSEN and T AAKHUS  | 167 |
| Angiography in duodenal carcinoma<br>By O OLSSON   | 177 |
| Arteriographic investigations of the normal hip in adults — Evaluation of methods and vascular findings<br>By H MÜSSBICHL  | 195 |

|   |     |
|---|-----|
| Submucosal haematoma of the oesophagus due to anticoagulant therapy — Report of a case  |     |
| By M. ANDRESS   | 216 |
| Retropertitoneal abscess with gas after perforation   |     |
| By L. E. HENRIKSSON   | 220 |
| Anatomic cause for intraossicular cavities in temporal bone tomography  |     |
| By B. SANDSTRÖM and H. F. WILBRAND  | 225 |
| Encephalography in the diagnosis of convexity block hydrocephalus   |     |
| By T. GREITZ and A. GREPE   | 232 |
| Lumbar myelography with water soluble contrast medium in children   |     |
| By R. STENSTRÖM and MARGARETA LINDFORS  | 243 |
| Centripetal descending phlebography in axillary vein thrombosis   |     |
| By U. BERGVAL   | 250 |
| Angiographic diagnosis of splenic lesions following blunt abdominal trauma  |     |
| By J. LEFASOON and T. OLIN  | 257 |
| Changes in vascular permeability after local application of roentgen contrast media in the hamster cheek pouch                                    |     |
| By S. E. SØRENSEN   | 274 |
| Spontaneous closure of arteriovenous fistulae following percutaneous renal biopsy — An experimental investigation in the rabbit                   |     |
| By L. EKELOUND  | 289 |
| Hemodynamic effect of contrast medium in arteriography of legs  |     |
| By E. BOIJSEN, J. DAHN and T. HALLBOOK  | 295 |
| Effect of iodinated roentgenographic contrast media on butanol-extractable, protein bound and total iodine in serum                               |     |
| By L. JACOBSSON and G. F. SALTZMAN  | 310 |
| Micturition urethrocytography in children with myelomeningocele — A radiologic and clinical investigation   |     |
| By N. O. ERICSSON, B. HELLSTRÖM, A. NERGÅRDH and U. RUDHE   | 321 |
| Angiography in renal failure  |     |
| By P. STAGE, E. BRIN, K. FOLKE and A. KARL  | 337 |
| Pleural fluid in healthy children   |     |
| By O. EKLÖF and A. TORNGREN   | 346 |
| Book reviews  | 350 |
| Angiography in rupture of the liver   |     |
| By T. AAKHUS and I. ENGE  | 353 |
| Angiography in hepatic rupture  |     |
| By E. BOIJSEN, J. KARLDE and U. TYLÉN   | 363 |
| Roentgenologic determination of the variations in heart volume during the cardiac cycle   |     |
| By K. BERGSTRÖM, L. BACKLUND and U. ERIKSSON  | 380 |
| Effect of water ingestion on spleen size as determined by radioisotope scans  |     |
| By J. D. PARKER and L. R. BENNETT   | 385 |
| Venous phase in spinal cord angiography   |     |
| By L. C. FRIED, J. L. DOPPMAN and G. DI CHIRO   | 393 |
| Effects of water soluble contrast media on the microcirculation in peripheral nerves — Registration of flow by microphotoelectric plethysmography |     |
| By S. E. SØRENSEN and M. ASANO  | 402 |



# Contents of Volume 11 — DIAGNOSIS

|  |     |
|--|-----|
| Electric potentials in pulmonary lesions — A preliminary report<br>By B NORDFÄSTRÖM  | 1   |
| Intraperitoneal contrast extravasation in lymphography<br>By P E ANDERSEN  | 17  |
| Defects in the urographic contrast medium above and below a ureteric calculus<br>By Ö ARNALDSSON and D HOLMLUND  | 26  |
| Repeat direct pyelography via needle nephrostomy<br>By R VELA NAVARRETT  | 33  |
| Arteriovenous fistulae following percutaneous renal biopsy<br>By L FRKLUND and T LINDHOLM  | 38  |
| Angiography in juxtacortical osteosarcomas — Case report with special reference to the differential diagnosis<br>By F P PRORST   | 49  |
| Effects of salicylates on the gastric mucosa as revealed by roentgen examination and the gastroscope<br>By D EDVÄR   | 57  |
| The adrenal glands after epinephrophlebography<br>By C G MIKÄELSSON  | 65  |
| Arteriography in arterial gunshot wounds<br>By J GIRL  | 78  |
| Excretion of sodium metrizoate through the liver during urography<br>By O OLSSON   | 85  |
| Relations between the cervical spine and the vertebral arteries<br>By P CONSTANTIN and C LUCRETIA  | 91  |
| Skeletal and tooth development — A methodologic investigation<br>By B LILIEQUIST and M LUNDBERG  | 97  |
| Percutaneous biopsy of vertebrae and ribs<br>By B NORDENSTRÖM  | 113 |
| Increased biliary concentration of contrast media by combined oral and intravenous administration<br>By M HÄVERLING, J SWEDENBORG and L THULIN                         | 122 |
| Ioglycamide (Bilivistan) as a contrast medium for intravenous cholangiography — A clinical and experimental investigation<br>By J BRISMAR, P LINDGREN and G F SALTZMAN | 129 |
| Phlebography in acute deep venous thrombosis of the lower extremity — A comparison between centripetal ascending and descending phlebography<br>By U BERGVAL           | 148 |
| Angiography in renal tuberculosis<br>By R BJÖRN HANSEN and T AAKHUS  | 167 |
| Angiography in duodenal carcinoma<br>By O OLSSON   | 177 |
| Arteriographic investigations of the normal hip in adults — Evaluation of methods and vascular findings<br>By H MUSSBACH   | 195 |

|   |     |
|---|-----|
| Fibromuscular hyperplasia and stationary waves of the internal carotid artery<br>By P R S KISHORE J P LIN and I I KRICHEFF                                  | 619 |
| Clinical and electroencephalographic sequelae of carotid angiography<br>By C D BINNIE, D C BERNSTEIN, A E BOOTH, I R MCCALL J H MARGERISON<br>and J F SCOTT | 626 |
| Transverse tomography with Mimer III<br>By K BERGSTROM L HOLMSTROM H LODIN O NYLEN and H WILBRAND   | 641 |
| Supplementary photographic technique — An aid in encephalography<br>By J I EISENMAN H F PRIBRAM and CECILE G JENKIN   | 650 |
| Head clamp autotomographic device for pneumography<br>By V TOLPESHNIKOV   | 653 |

|   |     |
|---|-----|
| Adverse reactions during urography and modification by atropine<br>By P SVINDSEN and J WILSON   | 497 |
| Phlebographic investigation of infusion thrombophlebitis<br>By U BERGVALI and A F FÄLUND  | 434 |
| Experimental roentgen examination of the vestibular aqueduct<br>By S BRUNNLR and CHR BRAHE PEDERSEN                                     | 443 |
| Broncho pulmonary vascular malformation syndrome causing left heart failure during infancy<br>By W MORTENSSON and N R LUNDSTRÖM         | 449 |
| Dyschondrosteosis<br>By K KOZŁOWSKI and C ZACHOWICZ   | 459 |
| Roentgen appearance of prostatic channels in infancy and childhood<br>By G THRANDER   | 467 |
| Large asymptomatic adrenal haematomas in the neonate<br>By O EÄLOF  | 481 |
| Angiography in dimethylnitrosamine induced rat renal tumours<br>By L FÄLUND and N JOHANSSON   | 489 |
| Stationary wave or segmental vasoconstriction<br>By E BERGQUIST, U ERIKSON and H R ULFENDAHN  | 497 |
| Diagnosis of gastric varices by conventional roentgenography as compared with splenoportal phlebography<br>By N GABRIELSSON             | 506 |
| Cervical phantom for evaluation of different methods of roentgen examination of the larynx<br>By A HEMMINGSSON                          | 515 |
| Perkutane Behandlung von Nierenzysten Die Tripelkontrast oder Pantopaque Methode<br>Von G W VESTBY                                      | 529 |
| Method of assessment of fetal weight<br>By H G RINGFRTZ   | 545 |
| Cinefluorography in demonstrating calcifications of mitral valves<br>By W MORTENSSON  | 553 |
| Gastric varices and phlebectases — A gastrophotographic and roentgenographic investigation<br>By N GABRIELSSON                          | 559 |
| Hydrostatic sialography as an index of salivary gland disease in Sjogren's syndrome<br>By D M CHISHOLM, G S BLAIR, P S LOW and K WHALEY | 577 |
| Delivery rates of certain contrast media through catheters for angiography and cardiography<br>By L BJÖRK, U ERIKSON and A HOLTZ        | 586 |
| Angiography of the hip region — Comparison between different angiographic modifications<br>By H MUSSBICHLER                             | 593 |
| Injection of contrast medium into unstained femoral lymph vessels for lymphography — A new technique and its indications<br>By O MYHRE  | 604 |
| Value of lymphography in the treatment of carcinoma of the vulva<br>By S HAGEN and R BJÖRN HANSEN                                       | 609 |

|   |     |
|---|-----|
| Centripetal descending phlebography in axillary vein thrombosis                               | 250 |
| Angiography of splenic lesions following blunt abdominal trauma                               | 257 |
| Vascular permeability after application of roentgen contrast media in the hamster cheek pouch | 274 |
| Spontaneous closure of arteriovenous fistulae following percutaneous renal biopsy             | 289 |
| Hemodynamic effect of contrast medium in arteriography of legs                                | 295 |
| Angiography in rupture of the liver   | 353 |
| Angiography in hepatic rupture  | 363 |
| Variations in heart volume during the cardiac cycle   | 380 |
| Venous phase in spinal cord angiography   | 393 |
| Phlebographic investigation of infusion thrombophlebitis                                      | 434 |
| Broncho pulmonary vascular malformation syndrome causing left heart failure during infancy    | 449 |
| Angiography in dimethylnitrosamine induced rat renal tumours                                  | 489 |
| Stationary wave or segmental vasoconstriction   | 497 |
| Diagnosis of gastric varices by conventional roentgenography and splenoportal phlebography    | 506 |
| Cinefluorography in calcifications of mitral valves   | 553 |
| Gastric varices and phlebectases  | 559 |
| Delivery rates of certain contrast media through catheters                                    | 586 |
| Angiography in the hip region   | 593 |
| Contrast medium injection into unstained femoral lymph vessels for lymphography               | 604 |
| Lymphography in the treatment of carcinoma of the vulva                                       | 609 |
| Fibromuscular hyperplasia and stationary waves of the internal carotid artery                 | 619 |
| Clinical and electroencephalographic sequelae of carotid angiography                          | 626 |

### Lungs, Pleura, Mediastinum and Chest walls

|  |     |
|--|-----|
| Electric potentials in pulmonary lesions   | 1   |
| Pleural fluid in healthy children  | 346 |
| Broncho-pulmonary vascular malformation syndrome causing left heart failure during infancy | 449 |

### Bones and Joints (incl soft tissue)

|   |     |
|---|-----|
| Angiography in juxtacortical osteosarcomas                      | 49  |
| Relations between the cervical spine and the vertebral arteries | 91  |
| Skeletal and tooth development                                  | 97  |
| Percutaneous biopsy of vertebrae and ribs                       | 113 |
| Arteriographic investigations of the normal hip in adults       | 195 |
| Dyschondrosteosis   | 459 |

### Ear, Nose and Throat

|   |     |
|---|-----|
| Intraossicular cavities in temporal bone tomography | 225 |
| Experimental examination of the vestibular aqueduct | 443 |
| Phantom roentgen examination of the larynx          | 515 |

## Subject index to Volume 11 — Diagnosis

## ROENTGEN DIAGNOSIS

## Nervous system

|  |     |
|--|-----|
| Relations between the cervical spine and the vertebral arteries                      | 91  |
| Encephalography in convexity block hydrocephalus                                     | 232 |
| Myelography with water soluble contrast medium in children                           | 243 |
| Micturition urethrocytography in children with myelomeningocele                      | 321 |
| Venous phase in spinal cord angiography  | 393 |
| Effects of water soluble contrast media on the microcirculation in peripheral nerves | 407 |
| Clinical and electroencephalographic sequelae of carotid angiography                 | 626 |
| Supplementary photographic technique in encephalography                              | 650 |
| Autotomographic device for pneumography  | 653 |

## Digestive tract (incl. biliary tract and spleen)

|   |       |
|---|-------|
| Intraperitoneal contrast extravasation in lymphography  | 17    |
| Effects of salicylates on the gastric mucosa  | 57    |
| Excretion of sodium metrizoate through the liver during urography                                 | 85    |
| Increased biliary concentration of contrast media by combined oral and intravenous administration | 122   |
| Ioglycamide (Bilivistan) as a contrast medium for intravenous cholangiography                     | 129   |
| Angiography in duodenal carcinoma   | 177   |
| Submucosal haematoma of the oesophagus  | 216   |
| Retroperitoneal abscess after perforation   | 220   |
| Angiography of splenic lesions following blunt abdominal trauma                                   | 257   |
| Angiography in rupture of the liver   | 353   |
| Angiography in hepatic rupture  | 363   |
| Effect of water ingestion on spleen size as determined by radioisotope scans                      | 385   |
| Asymptomatic adrenal haematomas in the neonate  | 481   |
| Diagnosis of gastric varices by conventional roentgenography and splenoportal phlebography        | 506   |
| Salivography as an index of salivary gland disease  | 577 ✓ |

## Heart and Vessels (incl. lymphatic vessels)

|   |     |
|---|-----|
| Intraperitoneal contrast extravasation in lymphography              | 17  |
| Arteriovenous fistulae following percutaneous renal biopsy          | 38  |
| Angiography in juxtacortical osteosarcomas                          | 49  |
| Adrenal glands after epinephrophlebography                          | 65  |
| Arteriography in arterial gunshot wounds                            | 78  |
| Relations between the cervical spine and the vertebral arteries     | 91  |
| Phlebography in acute deep venous thrombosis of the lower extremity | 148 |
| Angiography in renal tuberculosis                                   | 167 |
| Angiography in duodenal carcinoma                                   | 177 |
| Arteriographic investigations of the normal hip in adults           | 195 |

|   |     |
|---|-----|
| Centripetal descending phlebography in axillary vein thrombosis                               | 250 |
| Angiography of splenic lesions following blunt abdominal trauma                               | 257 |
| Vascular permeability after application of roentgen contrast media in the hamster cheek pouch | 274 |
| Spontaneous closure of arteriovenous fistulae following percutaneous renal biopsy             | 289 |
| Hemodynamic effect of contrast medium in arteriography of legs                                | 295 |
| Angiography in rupture of the liver   | 353 |
| Angiography in hepatic rupture  | 363 |
| Variations in heart volume during the cardiac cycle   | 380 |
| Venous phase in spinal cord angiography   | 393 |
| Phlebographic investigation of infusion thrombophlebitis                                      | 434 |
| Broncho-pulmonary vascular malformation syndrome causing left heart failure during infancy    | 449 |
| Angiography in dimethylnitrosamine induced rat renal tumours                                  | 489 |
| Stationary wave or segmental vasoconstriction   | 497 |
| Diagnosis of gastric varices by conventional roentgenography and splenoportal phlebography    | 506 |
| Cinefluorography in calcifications of mitral valves   | 553 |
| Gastric varices and phlebectases  | 559 |
| Delivery rates of certain contrast media through catheters                                    | 586 |
| Angiography in the hip region   | 593 |
| Contrast medium injection into unstained femoral lymph vessels for lymphography               | 604 |
| Lymphography in the treatment of carcinoma of the vulva                                       | 609 |
| Fibromuscular hyperplasia and stationary waves of the internal carotid artery                 | 619 |
| Clinical and electroencephalographic sequelae of carotid angiography                          | 626 |

### Lungs, Pleura, Mediastinum and Chest walls

|  |     |
|--|-----|
| Electric potentials in pulmonary lesions   | 1   |
| Pleural fluid in healthy children  | 346 |
| Broncho pulmonary vascular malformation syndrome causing left heart failure during infancy | 449 |

### Bones and Joints (incl soft tissue)

|   |     |
|---|-----|
| Angiography in juxtacortical osteosarcomas                      | 49  |
| Relations between the cervical spine and the vertebral arteries | 91  |
| Skeletal and tooth development                                  | 97  |
| Percutaneous biopsy of vertebrae and ribs                       | 113 |
| Arteriographic investigations of the normal hip in adults       | 195 |
| Dyschondrosteosis   | 459 |

### Ear, Nose and Throat

|   |     |
|---|-----|
| Intraossicular cavities in temporal bone tomography | 225 |
| Experimental examination of the vestibular aqueduct | 443 |
| Phantom roentgen examination of the larynx          | 515 |

### Uro-Genital system

|   |     |
|---|-----|
| Defects in contrast medium above and below a ureteric calculus                    | 26  |
| Repeat direct pyelography via needle nephrostomy                                  | 33  |
| Arteriovenous fistulae following percutaneous renal biopsy                        | 38  |
| Excretion of sodium metrizoate through the liver during urography                 | 85  |
| Angiography in renal tuberculosis   | 167 |
| Spontaneous closure of arteriovenous fistulae following percutaneous renal biopsy | 289 |
| Micturition urethrocytography in children with myelomeningocele                   | 371 |
| Urography in renal failure  | 337 |
| Adverse reactions during urography and modification by atropine                   | 477 |
| Prostatic channels in infancy and childhood                                       | 467 |
| Angiography in dimethylnitrosamine induced rat renal tumours                      | 489 |
| Perkutane Behandlung von Nierenzysten   | 579 |
| Assessment of fetal weight  | 545 |
| Lymphography in the treatment of carcinoma of the vulva                           | 609 |

### RADIOACTIVE ISOTOPES

|  |     |
|--|-----|
| Effect of water ingestion on spleen size as determined by radioisotope scans | 385 |
|--|-----|

### TECHNIQUE

|  |     |
|--|-----|
| Electric potentials in pulmonary lesions                   | 1   |
| Percutaneous biopsy of vertebrae and ribs                  | 113 |
| Phantom roentgen examination of the larynx                 | 515 |
| Delivery rates of certain contrast media through catheters | 586 |
| Transverse tomography with Mimer III                       | 641 |
| Supplementary photographic technique in encephalography    | 650 |
| Autotomographic device for pneumography                    | 653 |

### CONTRAST MEDIA

|   |     |
|---|-----|
| Excretion of sodium metrizoate through the liver during urography                                 | 85  |
| Increased biliary concentration of contrast media by combined oral and intravenous administration | 122 |
| Ioglycamide (Bilivistan) as a contrast medium for intravenous cholegraphy                         | 129 |
| Vascular permeability after application of roentgen contrast media in the hamster cheek pouch     | 274 |
| Hemodynamic effect of contrast medium in arteriography of legs                                    | 295 |
| Effect of iodinated roentgenographic contrast media on iodine in serum                            | 310 |
| Effects of water soluble contrast media on the microcirculation in peripheral nerves              | 402 |

### BOOK REVIEWS

|   |     |
|---|-----|
| Otorhinolaryngologic radiology — A radiologic atlas of ear nose and throat diseases | 350 |
| Golden's diagnostic radiology   | 351 |
| Radiologic examination of the colon   | 351 |
| Venography of the inferior vena cava and its branches                               | 352 |

## List of Authors

(r) indicates 'reviewed only'

- Aakhus T 167, 353  
 Andersen P E 17  
 Andress M R 216  
 Arnaldsson O 26  
 Asano M 402  
  
 Backlund L 380  
 Bennett L R 385  
 Bergquist E 497  
 Bergstrom K 380, 641  
 Bergvall U 148 250, 434  
 Bernstein D C 626  
 Binnie C D 626  
 Bjork L 586  
 Bjorn Hansen R 167, 609  
 Blair G S 577  
 Bojssen E 293, 363  
 Booth A E 626  
 Brahe Pedersen Chr 443  
 Brismar J 129  
 Brix E 337  
 Brunner S 443  
  
 Chisholm D M 577  
 Cimmino C V 351 (r)  
 Collins I C 351 (r)  
 Constantin P 91  
  
 Dahn I 293  
 Di Chiro G 393  
 Doppman J L 393  
 Dreyfuss J R 301 (r)  
  
 Edmar D 57  
 Eisenman J I 650  
 Ekelund L 38 289 489  
 Eklund A E 434  
 Eklof O 346 481  
 Enge I 353  
 Ericsson N O 321  
 Erikson U 380 497 586  
  
 Ferris E J 352 (r)  
 Folke K 337  
 Fried L C 393  
  
 Gabriellsson N 506, 559  
 Gurl J 78  
 Golden R 351 (r)  
 Greitz T 232  
 Grepe A 232  
  
 Hagen S 609  
 Hallbook T 293  
 Haverling M 122  
 Hellstrom B 321  
 Hemmingsson A 515  
 Henriksson L E 220  
 Hipona F A 352 (r)  
 Holmstrom L 641  
 Holmlund D 26  
 Holtz A 586  
  
 Jacobsson L 310  
 Janower M L 351 (r)  
 Jenkin Cecile G 650  
 Jonsson N 489  
  
 Kahn P C 352 (r)  
 Karle A 337  
 Kaude J 363  
 Kashore P R S 619  
 Kozlowski K 459  
 Krueff I I 619  
  
 Lepasoon J 257  
 Liliequist B 97  
 Lin J P 619  
 Lindfors Margareta 243  
 Lindgren P 129  
 Lindholm T 38  
 Lodin H 641  
 Low P S 577  
 Lucretia C 91  
 Lundberg M 97  
 Lundstrom N R 449  
  
 McCaul I R 626  
 Margerison J H 626  
 Mikaelsson C G 65  
 Mittermaier R 300 (r)  
  
 Mortensson W 449, 553  
 Myhre O 604  
 Mussbichler H 193, 593  
  
 Nergårdh A 321  
 Nordenström B 1, 113  
 Nylen O 641  
  
 Olin T 257  
 Olsson O 85, 177  
  
 Parker J D 385  
 Philips E 352 (r)  
 Prabram H F 650  
 Probst F P 49  
  
 Ringertz H G 545  
 Rudhe U 321  
  
 Saltzman G F 129, 310  
 Sandstrom B 225  
 Scott J F 626  
 Shapiro J R 352 (r)  
 Stage P 337  
 Stenstrom R 243  
 Swedenborg J 122  
 Svendsen P 427  
 Sorensen S E 274, 402  
  
 Theander G 467  
 Thulin L 122  
 Tolpeshnikov V 653  
 Torngren A 346  
 Tylen U 363  
  
 Ulfendahl H R 497  
  
 Vela Navarrete R 33  
 Vestby G W 529  
  
 Whaley K 577  
 Wilbrand H F 225, 641  
 Wilson J 427  
  
 Zychowicz C 459



# List of Supplements to Acta Radiologica

Nos 173—312

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For Suppl Nos 1—172 inclusive, see list issued December 1960, in Vol 54, fasc 6

The supplements are published from time to time and are not included in the subscription rate. Prices and year of publication of numbers already issued are detailed below.

- 173 ERIK ODEBLAD, BJÖRN WESTIN and SVEN ERIK ENGLUND Disappearance measurements. Theoretical, technical, biological and medical aspects 1959 Price Sw Kr 30
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## ELECTRIC POTENTIALS IN PULMONARY LESIONS

A preliminary report

by

BJÖRN NORDENSTROM

Cytologic and bacteriologic examinations of pulmonary tissues obtained by transthoracic needle biopsies have proved of considerable diagnostic value. Cytologic examinations permit differentiations to be made between benign and malignant tumours as well as between the types. Low differentiated cell forms indicate as a rule the presence of highly malignant growths and imply a poor prognosis. In spite of this, the roentgendagnostic and cytologic determinations

are of limited value in the prognosis. A further development of diagnostic means seems desirable and should perhaps not be restricted to morphologic studies, further diagnostic possibilities in morphology may well lie within the cytochemical and cytophysiologic fields.

Certain attempts have therefore been made to combine morphologic methods used in connection with transthoracic needle biopsy with microchemical and microphysiologic studies. Thus, the DNA of cell samples obtained at transthoracic needle biopsy has to some extent been studied in our department and the oxygen tension in different parts of malignant tumours in situ is now under investigation.

From the Thoracic Section of the Department of Diagnostic Radiology, Karolinska Hospital, Stockholm, Sweden. Presented at the Annual Meeting of the Society for Thoracic Radiology, Helsinki, June 1969. Submitted for publication July 1970.



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Fig 2



Fig 3

Fig 2 One electrode inserted into a bronchogenic carcinoma and one subcutaneously in the soft tissues of the chest

Fig 3 Two electrodes were first inserted into a neurolemmoma and irregular spikes were recorded. Then a third conventional needle was introduced. Small vital movements of the needle to provoke pain (—X—) produced only small superimposed waves

The assumption has been made in these investigations that variations in the electric tension of the individual pathologic cells may possibly also be reflected by a corresponding tension between a conglomeration of pathologic cells in the lung due to the fact that it is frequently surrounded by relatively low conducting pulmonary tissue

*Technique* Two different types of electrodes and registration instruments have been used. Only one of these techniques will however be described in the present report

The electrodes consist of 16 cm stainless steel biopsy needles (Fig 1) with an external diameter of 0.9 mm and an insulation layer of 0.05 mm teflon, only 2 mm of the needle tip and the proximal end of the needle were devoid of coating. Two electrode needles were connected to a standard electrocardiographic amplifier with a tungograph recording instrument (Elema). The time constant of the instrument was 1.3 seconds. The earthing cable was applied to the skin of the left arm of the patient by means of a standard electrode plate. Both measuring electrodes were in certain instances inserted into the pathologic tissue but generally only one of the electrodes was used for this purpose and the other was introduced subcutaneously in the vicinity of the insertion point of the first electrode (Fig 2).

The lung electrodes were inserted during videofluoroscopy. The position of the electrodes was documented by means of ordinary roentgenograms, or in certain instances, during their insertion, with cinefluorography in two perpendicular planes.



Fig 1 Stainless steel electrode biopsy needle of 1 mm external diameter including an insulating teflon layer. Needles of 9 to 16 cm length were used, 3 mm of the needle tip and connection piece are without teflon coating

A series of preliminary studies of the electric potentials of pulmonary lesions are now presented. The technical difficulties of electrode application and registration techniques and further the variability of the individual characteristics of the objects under investigation complicate the matter. The results in the present limited material should therefore be considered with the proviso that more extensive conclusions will be possible only after a series of investigations in large materials and with modification of the technique.

The different electric phenomena depend on the living cell. Electric potentials can be recorded in experiments *in vitro*, within the cell as well as across the cell membrane, the intracellular and transmembranous potentials thus simulate the polar tension of an electric battery, the 'liquid battery' of a cell obtaining its electric tension from the free radicals of the electrolytes. Various biologic and physical factors in the cell influence the migration and thus the location and concentration of the free radicals.

In diffusion, for example, a hydrogen ion migrates more rapidly than a chlorine ion, this causes the disturbance of the electric equilibrium that we call a diffusion potential. Diffusion occurs however not only within the cell but also through the cell membrane. The latter may on the other hand actively influence diffusion and thus modify the membrane potential. Factors such as specific ion permeability and oxidation and reduction sequences at the surface of the cell membrane may of course be of importance. Certain observations *in vitro* have indicated that the membrane potentials of rapidly growing cells may be considerably higher than those of slow-growing cells.

Unique and favourable conditions exist for a study of the disturbance of the electric potentials of pathologic tissues of the lung. From a physical point of view the air-containing lung tissue is a relatively good insulating medium and constitutes a prerequisite for an accurate application of the recording electrodes by means of videofluoroscopy.

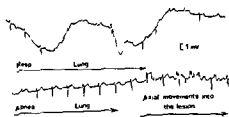
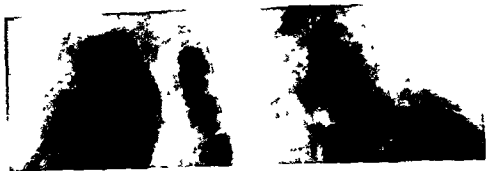


Fig 6

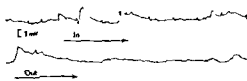


Fig 7

variations

Fig 7 Dense inflammatory lesion with central cavity. Insertion of the electrode needle into the periphery of the infiltration led to irregular small positive and negative potential variations

## Results

**Benign tumours** Transthoracic needle biopsy of neurofibromas always appears to give rise to pain that has come to be regarded as pathognomonic. The two teflon coated electrodes inserted in three cases into neoplasms that subsequently appeared to be neurolemmomas produced pain (Fig 3). The recording of the potential between the electrodes was in the nature of a continuous series of irregular spikes (approximate frequency 120/second). An ordinary biopsy needle inserted into the mass and turned in the malignant tissue failed to produce any change in the appearance of the spikes, small axial movements of the needle elicited only small movements of the base line. The appearance of the spikes in these cases may have been caused by pain impulses from the tumour. Up to now, only three neurolemmomas have been examined, all with the same type of irregular spikes. It should be noted however that interference from muscle potentials in the chest wall cannot yet be excluded as the source.

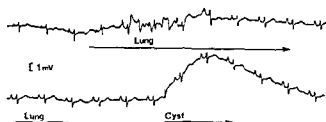


Fig 4



Fig 5

Fig 4 Puncture of a thin-walled pericardial cyst with the electrode produced a smooth positive potential followed by a slow return of the curve to zero (lung tissue) level. An amount of 20 ml of clear thin pericardial fluid were evacuated through the needle. Injection of a few milliliters water soluble contrast medium confirmed the diagnosis.

Fig 5 Insertion of the electrode into the rather tough solid tissue of a postinflammatory interlobal pleural thickening (pleuroma) produced a positive surface potential. A similar positive potential occurred when the electrode was withdrawn ('out ant').

Cell material from the pathologic tissue was taken for cytologic and bacteriologic examination in connection with the studies of the electric potentials. This was done in the manner described previously for the morphologic studies. The results of the investigation of the electric potentials were then compared with the results of the roentgenologic examinations and the microscopic analyses.

**Material** The following groups, comprising in all 107 cases, were studied, the verification being based on cytologic, bacteriologic and postoperative histologic examinations.

|   |    |
|---|----|
| Benign tumours (neurolemmoma 3, cysts 2)  | 5  |
| Inflammatory lesions (pleuroma 3, tuberculoma 9, fibrous tuberculous tissue 11, chronic non-specific inflammation 11, mycoma 2) | 36 |
| Metastases  | 12 |
| Bronchial carcinomas  | 47 |
| Non-verified lesions  | 7  |



Fig 10a



Fig 10b

Fig 10 a) Tumour like chronic inflammatory lesion with central cavity. Positive and negative potentials recorded on repeated insertions of the electrode. b) The main deflections in the bottom curve of (a) resemble the type of artefacts produced by the movement of an electric conductor in a magnetic field.

Fig 11 Unspecific inflammatory lesion. On insertion of the needle an initial negative deflection was obtained, followed by irregular positive deflections. When the electrode needle was thought to pass the posterior part of the infiltration a fresh negative deflection occurred. Small irregular deflections were observed when the electrode was withdrawn.

A similar type of curve was observed in a case of closed bronchial cyst filled with thin yellowish fluid.

*Inflammatory lesions.* The insertion of one electrode needle into a pleuroma interlobar thickening of the pleura (Fig 5) gave rise to a well defined peak at and a small negative potential under the surface of the lesion; a small negative potential was recorded in its centre. When the electrode needle was withdrawn a mirror-like potential response was recorded.

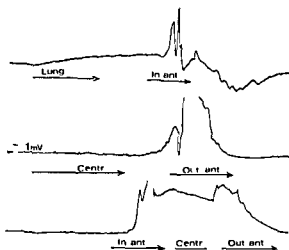


Fig 8

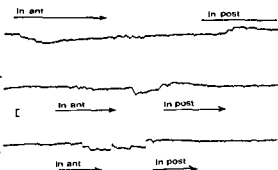


Fig 9

Fig 8 Tuberculoma. The three curves represent needle inserted into the tuberculoma (top) needle withdrawn (middle), needle inserted and withdrawn, i.e. a composition of the two curves (bottom). A positive surface potential occurs in all three tracings the negative potential in the tuberculoma in the top curve may have been hidden due to the recording technique.

Fig 9 Non specific inflammatory lesion. Only small negative potentials were recorded on insertion into the lesion when the needle passed out through the posterior aspect of the lesion ('in post') minimal positive curve deflections were recorded.

*Pericardial cyst* A bulging contour of the right side of the heart is seen in Fig 4. As it appeared to possess all the features of a pericardial cyst it was punctured with the needle electrode during registration of the electric potentials. Irregular variations in the curve occurred during the passage through the lung tissue (upper curve in Fig 4) apart from the LCG potentials. Puncture of the thin-walled cyst produced a smooth positive deflection with a slow return to zero (lung tissue) potential and 20 ml of clear thin pericardial fluid was removed through the needle electrode. Then a few milliliters of a water-soluble contrast medium were injected into the cyst and the preliminary diagnosis of a pericardial cyst was confirmed.

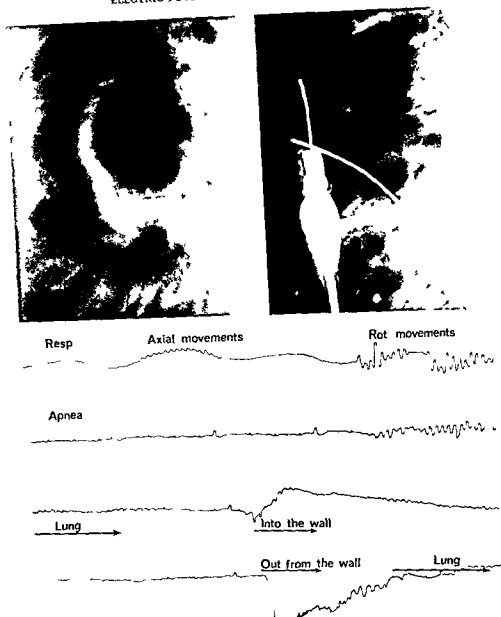


Fig 12 Blastomycoma. One electrode was inserted into the wall of the lesion and a second electrode into the lung. On small axial movements or rotational movements of the second electrode small curve deflections were recorded (the two top curves). When the second electrode was inserted into the wall of the lesion during apnea a positive curve deflection was obtained (third curve). A similar negative deflection was obtained upon withdrawal of the electrode from the lesion (bottom curve).



Fig 6 is from a case of an old fibrous inflammatory infiltration of the right upper lobe. When the electrode was kept in the apparently normal lung tissue, the base line moved synchronously with respiration (upper curve). No variations apart from those from the ECG occurred (lower curve) when the needle was advanced during apnea. Only small irregular variations were noted when axial movements were produced with the needle in fibrotic lung tissue.

Fig 7 also represents an inflammatory lesion but this had a more dense tissue than the previous one. An irregular wave-like curve was obtained in the tracing of the electric potentials with the electrode.

Fig 8 is of a well-defined inflammatory lesion of 'compact' tissue material, a tuberculoma. The upper curve indicates the potential variations when the electrode needle was inserted into the lesion. A positive peak potential is seen, followed by a clearly negative potential, with slow return to approximately zero level. The middle curve represents the removal of the needle from the inner part of the tuberculoma and the lowest curve the insertion and withdrawal of the needle. The lowest curve appears to represent a combination of the two upper curves. All the curves present positive potentials apparently correlated to a surface potential. The negative potential in the tuberculoma (top curve) may however be hidden as a result of the recording technique (middle and lower curves).

The non-specific inflammatory lesion in Fig 9 is an example of the entirely negative potentials sometimes obtained on insertion of the electrode. Only minute positive potentials could be recorded when this passed out through the posterior part.

Fig 10 represents an inflammatory mass with central necrosis and a cavity containing air. On repeated insertion of the electrode into the wall through the cavity and the posterior wall a regular pattern of electric potential deflections was obtained. The positive deflections represent the periphery of the infiltration and the negative deflections in the upper record the central cavity. The main deflections of the lower curve in Fig 10a resemble the type of artefacts produced by the movements of an electric conductor in a magnetic field, as illustrated in Fig 10b.

An unspecific inflammatory lesion is seen in Fig 11. Negative deflections were obtained at the periphery of the lesion, its dense part presented however mainly positive deflections.

A blastomycoma is shown in Fig 12. After the introduction of an electrode into the wall of the lesion, the second electrode was inserted during recording of the electric potentials. Respiratory variations with superimposed small curve variations occurred in the lungs (upper two curves) when the electrode was moved axially or with small rotational movements. When the electrode was

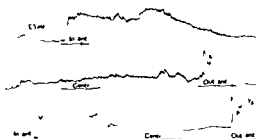


Fig 15

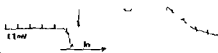


Fig 16

Fig 15 Necrotic (upper) and with are represented in tracings. The nec

The long lasting elevation of the curve at the insertion mainly depends on the slower advance of the needle as compared to the withdrawal. The high frequency variations in the upper two tracings may be due to muscle potentials recorded via the chest wall electrode.

Fig 16 Squamous cell anaplastic small-cell carcinoma with cavity formation. Negative and positive potentials were recorded. In spite of the relatively small size of the tumour the potential response on insertion of the needle was such that it prevented registration of the whole curve.

**Malignant tumours** The large metastatic melanomasarcoma represented in Fig 13 appeared to be partly necrotic. Small negative potentials were recorded in the tumour in relation to the zero level represented by the lung tissue potential.

Positive and negative deflections may be recorded in primary bronchial carcinomas. The relatively large squamous cell carcinoma seen in Fig 14 subsequently proved to be partly necrotic. The insertion of the needle into the mass revealed a high positive wall potential and possibly also some negative potentials (upper curve) as well. By advancing the electrode towards the posterior wall of the tumour a distinct negative potential deflection was first obtained which however turned into a high positive potential when the needle reached the wall (lower curve). It should be noted that the potential deflections were of a magnitude

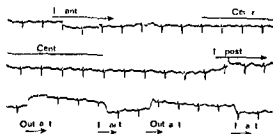


Fig 13

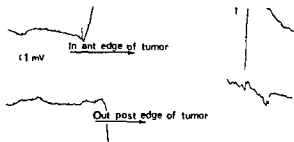


Fig 14

Fig 13 Metastatic melanoma with central necrosis. Only small negative potential variations were recorded when the electrode was inserted. The tracing returned to zero (lung) potential when the electrode perforated the posterior tumour wall or was withdrawn from the mass.

Fig 14 Low differentiated necrotic bronchial carcinoma. When the needle reached the tumour edge a high positive potential was recorded (upper curve). In spite of the lowest possible amplification the registration instrument could not trace the whole curve. When the needle was advanced into the mass a strong negative deflection was followed by a high positive deflection as the posterior wall of the tumour was reached (bottom curve).

advanced against the wall of the mycoma, a positive potential with slow return to zero (lung tissue) level was recorded. A similar but negative deflection was obtained (lowest curve) when the electrode was withdrawn.

*Comments.* These cases of inflammatory lesions illustrate that relatively small positive and negative potentials may occur in slightly 'condensed' pulmonary tissue. Higher positive and negative potentials were observed in well demarcated 'tumour-like' tissue. It seems possible that negative potentials in inflammatory lesions indicate the presence of destruction, negative potentials have also been recorded in necrotic malignant lung tissue, as will be reported below.

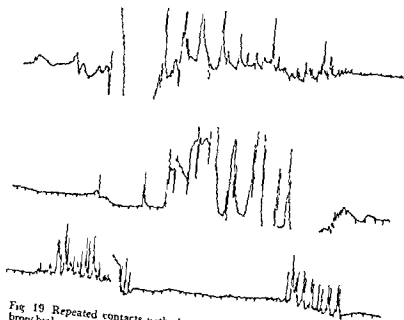


Fig 19 Repeated contacts with the electrode tip against the surface of a bronchial carcinoma produced a clearly decreasing potential response (upper curve) and the same manoeuvre against the surface of a tuberculoma also tended to decrease the potential response (middle and bottom curves). The decreasing potential responses on repeated electrode contact with the surface of the two types of lesions may be explained by an electric discharge of the lesions.

The squamous-cell anaplastic small cell carcinoma in Fig 16 had a diameter of 3 to 4 cm and contained necrotic material in the centre. Negative and positive potentials were recorded on insertion of the electrode. In spite of the relatively small size of the mass the potential responses were of a magnitude that did not allow tracing of the whole curve.

The recording of the electric potentials in the low differentiated squamous cell carcinoma of Fig 17 presents a striking contrast to the previous case, repeated insertions of the electrode produced only minimal irregular deflections.

The low differentiated squamous cell carcinoma in Fig 18 was roughly of the same size as the lesions in the two previous cases. Surface potentials were recorded (see Fig 17). The upper curve indicates variations on the slow advance of the electrode and the lower curve its more rapid movement. The movements of the electrode in this case were correlated to the curve deflections during cine-radiography. Two perpendicular film projections with alternating pulsed exposures and 48 frames per second in each projection were used. The instant of exposure was marked (see lowest curve).

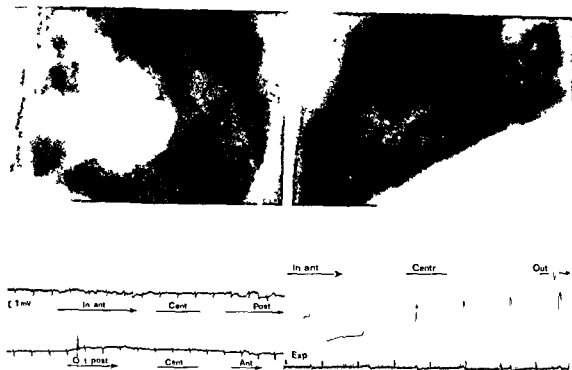


Fig 17

Fig 18

Fig 17 Low differentiated squamous cell carcinoma. On insertion of the needle into the tumour (in ant) as it lay within it and as it passed through the posterior wall only small potential deflections were recorded (upper curve). On withdrawal of the needle (bottom curve) similar small deflections were recorded from the posterior wall of the mass (out post) in the centre and from the anterior wall (ant).

Fig 18 Low differentiated squamous cell carcinoma. A positive potential was recorded as the needle perforated the wall of the tumour. A new potential response was obtained from the wall (out ant) upper curve) as the needle was withdrawn. Similar wall potentials were recorded (bottom curve) on repeated insertions and withdrawals of the needle. The movements of the needle in this case were correlated to the curve deflections by means of cineradiography.

that did not allow the registration of the whole event in spite of the lowest possible amplification.

Fig 15 is from a low-differentiated squamous cell carcinoma that was punctured at the periphery to avoid the obviously necrotic centre. A relatively high positive potential was recorded at the insertion (upper curve) and a positive potential when the needle was retracted from the wall (middle curve). The lowest curve represents the same procedure performed somewhat more rapidly. Certain characteristics may be identified in the two tracings. The long lasting elevation of the curve at the insertion is mainly a result of the slower advance of the needle compared to its withdrawal. The high frequency variations in the upper two tracings may be due to muscle potentials recorded via the chest wall electrode.

# ELECTRIC POTENTIAL IN PULMONARY LESIONS

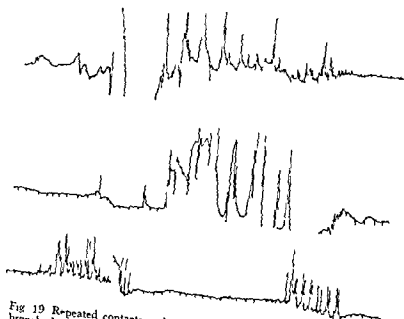


Fig 19 Repeated contacts with the electrode 1 p against the surface of a bronchial carcinoma produced a clearly decreasing potential response (upper curve) and the same manoeuvre against the surface of a tuberculoma also tended to decrease the potential response (middle and bottom curves). The decreasing potential responses on repeated electrode contact with the surface of the two types of lesions may be explained by an electric discharge of the lesions.

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*Comments* Negative potentials have been observed in the presence of necrotic changes in malignant tumours as well as in inflammatory lesions. The preliminary impression is that the negative potentials indicate the presence of damaged tissue.

The magnitude of the potential response in a bronchial carcinoma bears no clear relation to the actual size of the mass. The tumour in Fig. 16 was considerably smaller than the one represented in Fig. 15. In spite of this the potential response at the insertion of the electrode was at a level that did not even allow the instrument to record the whole curve from the small tumour. The magnitudes of the potential responses in bronchial carcinomas have often been more than 12 mV, the maximum for the recording instrument.

The highest positive and negative potentials have been observed in cases of malignant growths. The recordings from low differentiated squamous cell carcinomas have indicated a remarkably low potential response. This has been seen in spite of the fact that the cytologic type and degree of differentiation have borne a striking similarity to other malignant tumours with high potential response.

*A condenser theory for pulmonary lesions* The discrepancy in the magnitudes of potential responses between some cytologically identical malignant tumours gave rise to the assumption that any kind of solid tissue in the lung may act as an electric condenser. A tuberculoma, a malignant tumour, an interlobar pleuroma or any other solid formation in the lung surrounded by the low conducting pulmonary tissue may obtain an electric charge either from surrounding tissue potentials or from action potentials produced in the lesion.

A support for the condenser theory may be that high potentials frequently occur at the surface of well demarcated tumour like lesions.

It was also observed that the highest potentials were recorded at the first contact of the electrode with a solid lung lesion. It was then noted that the surface potentials often decreased in magnitude after repeated puncture. The possibilities of a discharge of the surface tension was therefore investigated.

A recording from a bronchial carcinoma while a picking movement was made with the electrode against the surface of the tumour is presented in Fig. 19 (upper curve). It can be seen that the amplitude of the potential clearly decreased. The same manoeuvre was made against a tuberculoma as represented in the middle and lower curves of Fig. 19; also here the record shows a decreasing potential. These observations were made repeatedly in the series when the initial surface potential was high. The decreasing potential response can however only in certain lesions be brought down to a given level (resting potential) with the present technique. Whether this may be due to the technique being insufficient

to discharge the lesion or to the effect of continuous action potentials are matters for further investigation

### Conclusions

The needles used in connection with the basic technique of transthoracic needle biopsy have been modified and utilized for recording the electric potentials of various pulmonary lesions. It has been found that a great variety of electric phenomena can be recorded *in situ* in inflammatory and neoplastic pulmonary lesions. The electric phenomena that are encountered seem to offer new aspects on the functional and biophysical states in different lung conditions. The present report has been limited to the description of certain general impressions.

Irregular high frequency potentials were recorded in intrathoracic neurinomas and positive potentials were usually observed in inflammatory lesions and some times in malignant tumours. Negative potentials seemed to indicate the presence of damaged tissue or an air space. Aspiration of cell material from tumour regions presenting negative potentials often revealed necrotic or non diagnostic material. Well demarcated masses in the lung, such as tuberculomas and small peripheral carcinomas, often had a distinct, high surface potential with lower or even negative potentials in the centre. Some inflammatory lesions and malignant tumours presented dominating negative potentials. Bronchial carcinomas usually had a high ( $> 12$  mV) surface potential ( $12$  mV = maximum capacity of the recording instrument) and others presented zero potentials. A decreasing surface potential response may be obtained by repeated contact between the electrode and the surface of a lesion with a high surface potential. This artificial discharge has as yet not been observed to reach zero level (final surface potential or resting potential).

An attempt has been made, on the basis of the observations made on the surface potentials, to explain some of the seemingly contradictory results by means of a preliminary condenser theory for certain pulmonary lesions.

### SUMMARY

A preliminary investigation in 107 patients suggests that certain characteristics may be extracted for different groups of pulmonary lesions. The recording of electric potentials *in situ* seems to offer new functional and biophysical aspects in lung pathology. The technique for introduction of biopsy needles into the lung previously described by the author has now, after modifying the needles, been employed to record electric potentials in the lung tissue as well as to collect samples of cell material.



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The highest positive and negative potentials have been observed in cases of malignant growths. The recordings from low-differentiated squamous cell carcinomas have indicated a remarkably low potential response. This has been seen in spite of the fact that the cytologic type and degree of differentiation have borne a striking similarity to other malignant tumours with high potential response.

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## INTRAPERITONEAL CONTRAST EXTRAVASATION IN LYMPHOGRAPHY

by

POLL E. ANDERSEN

The increasing use of lymphography during the last decade in the clinical investigation of systematic lymphatic diseases, as well as in the search for malignant metastases, particularly from genito-urinary carcinomas, has augmented our knowledge of the anatomy and physiology of the lymphatic vascular system. The filling of perhaps hidden collaterals and anastomoses, whether pre-existing or newly formed, may explain many cases of unusual metastases in unexpected regions.

Extravasation of lymph or chyle, or both, into existing cavities, or the creation of cyst like collections of lymph, have been reported by many authors and constitute several well known syndromes. The extravasation may take place into the peritoneal cavity, the renal pelvis, the intestines, the liver, the pericardium and the pleural cavities, syndromes that have all been demonstrated by lymphography during the last decade (KITREDGE et coll 1963, SWANSON 1963, BOURDON et coll 1964, CAMIEL et coll 1964, ISHIDA et coll 1965, COLLETTE et coll 1967, GRUWEZ et coll 1967, MACDONALD 1967, BUCHHEIT et coll 1967, TAKAHASHI et coll 1968, AKISADA et coll 1968 and DANIEL et coll 1969). The point of blockage of lymph vessels has been revealed by lymphography and often made it possible to demonstrate the leakage of contrast medium.

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## ZUSAMMENFASSUNG

Eine vorläufige Untersuchung an 107 Patienten lässt vermuten, dass gewisse Charakteristika für verschiedene Gruppen von Lungenläsionen abgegrenzt werden können. Die Registrierung von elektrischen Potentialen *in situ* scheint neue funktionelle und biophysikalische Aspekte in der Lungenpathologie darzubieten. Die Technik Biopsie Nadeln in die Lunge einzuführen wie sie früher vom Verfasser beschrieben worden ist ist jetzt nach Abänderung der Nadeln verwendet worden elektrische Potentiale des Lungengewebes zu registrieren und gleichzeitig Gewebeproben zu entnehmen.

## RÉSUMÉ

Une recherche préliminaire sur 107 sujets fait penser que l'enregistrement des potentiels électriques pulmonaires permet de reconnaître des caractéristiques de différents groupes de lésion. L'enregistrement de potentiels électriques *in situ* paraît offrir des données fonctionnelles et biophysiques nouvelles dans la pathologie pulmonaire. La technique d'introduction d'aiguilles de biopsie dans le poumon déjà décrite par l'auteur a été utilisée après modification des aiguilles pour enregistrer les potentiels électriques dans le tissu pulmonaire et pour faire des prélèvements de cellules.

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parenchyma in most of the cases reported. In some cases, contrast medium has been seen passing through a retrosternal route to fill a few internal parasternal lymph nodes (HANSEN 1969, ANDERSEN 1969).

Leakage of oil contrast medium either from tumour surfaces or of iatrogenic origin into the abdominal cavity was observed in three cases without concomitant ascites or chyloperitoneum. These rare cases were encountered within 2 years so that their publication appears justified.

### Case reports

*Case 1* Woman aged 56 with a solid irregular granulosa cell carcinoma the size of an orange present in the right ovary at appendectomy 3 years previously.

Bilateral salpingo-oophorectomy believed to be radical in spite of some invasion of the parietal peritoneum at the site of the tumour was performed. Excised paracaval lymph nodes failed to reveal metastases at microscopy. The patient had post-operative cobalt therapy with a dose of 5500 R to the tumour site and was well for 15 months.

Gynecologic examination 15 months later when she was without any symptoms disclosed firmness but no definite infiltration or growth in the right parametrium. The patient returned 10 months later complaining of lumbar pain radiating to the right kidney region and the right iliac fossa and with increasing edema of the right leg. The gynecologic examination was almost identical but roentgen examination including tomography of the lumbar spine, revealed osteolytic metastases in the right lamina of the vertebral arch of the fifth lumbar vertebra and intravenous urography indicated compression of the right ureter at the linea terminalis pelvis.

*Lymphography* revealed on the left side a few trunks passing along the iliac vessels to the aortic bifurcation. On the right side a faint network resembling collaterals ran along and around the iliac vessels and soon branched off in numerous collaterals in the right posterolateral part of the pelvis and anterior to the sacrum. On reaching the level of the promontory contrast medium began seeping into the peritoneal cavity (Fig. 1a), and in the 24 hour film (Fig. 1b) a considerable amount of medium coated the cecum and terminal ileum as well as the surface of the liver similar to the appearances in hysterosalpingography. No normal lymphatic trunks could be followed above the bifurcation level but on late films left supraclavicular nodes and a single retrosternal node were present to indicate passage of the contrast medium via collaterals.

At exploratory laparotomy 3 weeks later no fluid was present in the peritoneal cavity. A firm infiltrating plaque measuring 3 cm × 2 cm with a thickness of 3 to 4 mm was revealed in the right part of the pelvis at the compressed portion of the ureter. Several enlarged lymph nodes were felt to the right of L4 and L5 but no peritoneal or hepatic metastases could be demonstrated. Biopsy from the infiltration and the lymph nodes disclosed metastatic granulosa cell carcinoma. The condition of the patient deteriorated and she died some time after chordotomy had been performed.

*Case 2* Woman aged 42 years, gynecologic department. Her enlarged uterus on biopsy disclosed adenocarcinoma.

The patient was treated by total hysterectomy and bilateral salpingo-oophorectomy. A



Fig. 1 Case 1 a) Oblique view Extravasation of contrast medium in the right pararectal fossa and along the linea terminalis pelvis b) Film obtained 24 hours later Abundance of contrast medium between intestinal loops No lymph nodes or vessels visible at L4

Among the more common causes of blockage and retrograde flow of contrast medium should be mentioned trauma to the cisterna chyli and the thoracic duct (GRUWEZ et coll 1967) either iatrogenic or by penetrating or external blunt injury, mechanical obstruction, e.g. by filaria or other parasites (MONTANCERAND et coll 1965, KOEHLER et coll 1968, AKISADA et coll 1968), abdominal para-aortic or mediastinal malignant disease (FUCHS & ZUPPINGER 1965, ISHIDA et coll 1965, BUCHHELT et coll 1967), or congenital anomalies (LEVINE 1961, CRAVEN et coll 1967). Extensive reports and analyses have been given by e.g. GROVES et coll (1954), NIX et coll (1957), KELLEY et coll (1960), BOURDON et coll (1964, 1967), CHOI et coll (1964), MACDONALD (1967), COLLETTE et coll (1967), while experimental clinical and laboratory investigations were carried out by POMERANTZ et coll (1963), NEYAZAKI et coll (1965), and TAKASHIMA et coll (1966).

Seepage of chyle into the peritoneal cavity, creating chyloperitoneum or chylous ascites may occur in total or partial obstruction of the cisterna chyli and the thoracic duct. No passage of contrast medium through the thoracic duct occurred and none was visible in the left supraclavicular region or in the lung



Fig 3 Case 2 Film obtained 24 hours later than the one in fig 2 Contrast medium is present in the right pararectal fossa and between the coils of intestines

Larger amounts of contrast medium were seen at 24 hours (Fig 3) but now mainly in the right part of the pelvis. There was no sign of intraperitoneal fluid and the thoracic duct was intact.

A barium enema revealed malignant invasion of the sigmoid colon and intravenous urography disclosed a white left kidney with the pelvis and calyces almost indistinguishable for 24 hours. The patient had palliative betatron therapy with good effect on pain and tumour size but six weeks after completion of the treatment a rapid decline in the general condition began and the patient died within 2 months. No autopsy was performed.

**Case 3** Woman aged 66 with a history of a few episodes of hematuria, had a bladder tumour located around the left ureteral ostium and diagnosed by intravenous urography.

Lreterocystoneostomy was performed and the growth was radically extirpated. Histologic examination of the mass revealed carcinoma without definite invasion of the peripheral layers of the bladder.

The tumour

to the r

the left

the left pelvic wall. Intravenous urography disclosed moderate left hydronephrosis and hydro-ureter with slightly impaired function, confirmed by isotope renography. Angiography of the bladder revealed malignant tissue with pathologic vessels and slight loading corresponding to the findings on exploration.



Fig 2 Case 2 Blockage in the left inguinal and sacro iliac regions numerous collaterals around and in the bladder wall small amounts of intra peritoneal contrast medium are present Cf fig 3

10 cm $\times$ 10 cm tumour, firm and irregular lay in the right part of the anterior uterine wall. The peritoneum was intact but a 3 cm $\times$ 3 cm hard and fixed lymph node was felt on the left pelvic wall. No metastatic glands were evident else where in the pelvis or along the aorta. The liver was normal without palpable or visible metastases. Biopsy from the enlarged lymph node was negative.

Rectovaginal exploration 3 months after completion of postoperative cobalt 60 therapy revealed a firm triangular infiltrate fixed to the left pelvic wall which on control 2 months later had increased and was hard and irregular. The patient then began to complain of feeling very tired. She suffered from phlebitis of the left leg and intractable pain in the left inguinal and sacral regions. On palpation a large tumour was felt just above the left inguinal ligament. Isotope renography disclosed impaired emptying of the left renal pelvis and upper part of the ureter. The sedimentation rate had risen from 15 mm to 101 mm/hour and the alkaline serum phosphatases were markedly increased.

*Lymphography* indicated partial blockage of the lymph vessels from the femur in the left inguinal region with cystic dilatation of the afferent lymph vessels and later perilymphatic extravasation of contrast medium (Fig 2). Some few vessels from this area of blockage passed to nodes below the excised lymph node where further blockage was observed. Numerous collaterals were seen around the bladder. Shortly after the contrast medium had reached the level of the left sacro iliac joint some of it lay free in the peritoneal cavity presumably seeping from a lymph vessel in the left pararectal fossa. No abnormality was present on the right side.

thoracic duct, the left supraclavicular region, and in the lung parenchyma with the typical reticular pattern FUCHS (1967) reported a case of a 47-year-old woman with a stage III cervical cancer without ascites or chyloperitoneum, and TAKAHASHI *et coll* (1968) published one case of a 71-year-old woman with reticulosarcoma, who had oil contrast medium in the peritoneal cavity but no chyle, oil medium could, however, not be demonstrated in the lungs in these cases

The present three cases occurred among approximately 600 lymphographies, giving an overall incidence of about 0.5 per cent. Leakage was localized to a point of recurrence of the malignant disease, most of the contrast medium passing either through the normal route or via collaterals to the cisterna chyli. The lymphographic appearances in our Case 1 were altered by the bilateral salpingo-oophorectomy followed by cobalt therapy. As no stasis was observed in the fine lymph vessels in the right part of the pelvis it is probable that the contrast medium seeped from the infiltrated area, which was verified 3 weeks later at exploratory laparotomy, particularly as the first point of appearance of the medium between the intestinal loops was at the sacral promontory, well above the previous operation area. The fact that no droplets were formed, but merely a coating of the intestines was produced, indicated that the amount of fluid in the peritoneal cavity was insignificant, thus confirming the absence of ascites.

The extravasation of contrast medium in Case 2 apparently took place at a level, corresponding with the compression of the left ureter and the infiltrate felt at the gynecologic examination. The leak in Case 3 was at the infiltrated area that had twice been operated upon. This raises the question of the *mechanism* of contrast medium seepage. It is hardly probable that the operative intervention itself could have caused the leakage, as the operation area in Cases 1 and 2 was at some distance from the site of appearance of the contrast medium. That lymphatic vessels should remain open and 'bleeding' for more than 2 years after the operation, as in Case 1, is likewise improbable and contradicted by the *absence of fluid* in the peritoneal cavity. It seems more likely that the para iliac lymphatic trunks were invaded and destroyed by the malignant metastatic tissue, or that they anastomosed with lymph vessels or intercellular spaces in the growth. This made possible a 'bleeding' of lymph from the tumour surface, similar to the faint hemorrhage manifested by the well known hemorrhagic fluid in primary or metastatic malignancy of the pleura and peritoneum. Unfortunately, no attempt was made during the operation in Case 1 to demonstrate, for instance by the injection of dye into the para iliac lymphatic trunks, the point of leakage or extravasation from the surface of the malignant plaque.

The absence of visible peritoneal spread of the malignant disease may perhaps be taken as a sign that it is not malignantly infiltrated lymph vessels that bleed but





Fig 4 Case 3 a) Partial blockage in left iliac fossa with numerous perivesical collaterals slight amount of intraperitoneal contrast medium b) Film obtained 24 hours later There is contrast medium between the intestinal loops and filling of right para iliac nodes via the perivesical collaterals

The patient was again subjected to operation with extirpation of the metastatic gland and re ureterocystoneostomy. Microscopy of the removed portion of the left ureter disclosed carcinoma. No ascites or chyloperitoneum were found at operation.

Two months later the patient was readmitted in fair condition with normal kidney function and without demonstrable ascites but with large pelvic, extravascular masses.

Lymphography revealed partial blockage of the lymphatic vessels in the left inguinal region and left part of the pelvis with stagnation and extravasation of contrast medium in the perilymphatic tissue (Fig 4 a). Numerous collaterals were filled in and around the bladder as well as posteriorly. At the site of the removed metastatic lymph node, contrast medium leaked into the peritoneal cavity, and on the following day a large amount lay intraperitoneally with appearances similar to those produced at Lipiodol hysterosalpingography (Fig 4 b). Some contrast medium passed into the left para iliac lymph vessels and via collaterals on the right side (no medium was introduced via the right leg) with filling of para aortic nodes and the thoracic duct. No definite metastases were observed in the lumbar nodes. The lungs had a typical reticular contrast medium pattern.

Cobalt 60 therapy was initiated but the patient died suddenly 3 weeks later. Autopsy failed to reveal the cause but confirmed the malignant condition and spread of the disease.

### Discussion

Extravasation of oil contrast medium into the peritoneal cavity with intact, functioning cisterna chyli and thoracic duct seems to be rare. In such cases there is no chyle in the abdominal cavity, while contrast medium appears in the

thoracic duct, the left supraclavicular region, and in the lung parenchyma with the typical reticular pattern. FUCHS (1967) reported a case of a 47-year-old woman with a stage III cervical cancer without ascites or chyloperitoneum, and TAKAHASHI *et coll* (1968) published one case of a 71-year-old woman with reticulosarcoma, who had oil contrast medium in the peritoneal cavity but no chyle, oil medium could, however, not be demonstrated in the lungs in these cases.

The present three cases occurred among approximately 600 lymphographies, giving an overall incidence of about 0.5 per cent. Leakage was localized to a point of recurrence of the malignant disease, most of the contrast medium passing either through the normal route or via collaterals to the cisterna chyli. The lymphographic appearances in our Case 1 were altered by the bilateral salpingo-oophorectomy followed by cobalt therapy. As no stasis was observed in the fine lymph vessels in the right part of the pelvis it is probable that the contrast medium seeped from the infiltrated area, which was verified 3 weeks later at exploratory laparotomy, particularly as the first point of appearance of the medium between the intestinal loops was at the sacral promontory, well above the previous operation area. The fact that no droplets were formed, but merely a coating of the intestines was produced, indicated that the amount of fluid in the peritoneal cavity was insignificant, thus confirming the absence of ascites.

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It is perhaps  
 but - - - - -  
 or malignantly infiltrated lymph vessels that bleed but

that vessels burst on account of the blockage of their paths, as demonstrated by the stasis and the collaterals in all three cases

Whatever the mechanism may be, the occurrence of extravasation of contrast medium into the peritoneal cavity must carry a poor prognosis, similar to that in cases of extralymphatic extravasation described by, among others, ROCFERS & AMORY (1969). These authors regarded the sign as indicating advanced disease with destruction of the lymph node and its capsule. This mechanism may have been the true one in Case 3, in which extralymphatic extravasation was also noted in the inguinal region, and in which operative and histologic verifications of malignant invasion of the pelvic lymph nodes were obtained.

No definite conclusion on the mechanism of extravasation of contrast medium can be drawn from the material but it appears probable that stasis and the bursting of lymph vessels prior to blockage by malignant tissue is a frequent cause and that the prognosis following such leakage must be considered bad.

## SUMMARY

Three cases of extravasation of contrast medium into the peritoneal cavity at lymphography at which the cisterna chyli and thoracic duct were intact are described.

## ZUSAMMENFASSUNG

Es wird über drei Fälle berichtet in denen Extravasation von Lymphographiekontrast trotz funktionierender Cisterna chyli und Ductus thoracicus beobachtet wurde.

## RÉSUMÉ

Description de trois cas d'extravasation du moyen de contraste dans la cavité péritonéale au cours d'une lymphographie alors que la citerne de Pecquet et le canal thoracique étaient intacts.

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## DEFECTS IN THE UROGRAPHIC CONTRAST MEDIUM ABOVE AND BELOW A URETERIC CALCULUS

by

ÖRN ARNALDSSON and DAN HOLMLUND

The aim of the present investigation was to study the frequency of contrast medium defects in routine urograms just above and just below a ureteric stone, and to correlate the findings with the size and position of the calculus. The clinical value of a demonstration of these roentgenologic signs will be discussed.

*Contrast medium defects just above a ureteric calculus* The urine above a ureteric calculus contains salts, red and white cells, mucoprotein and cells from the ureteric and pelvic mucosa and is usually cloudy. This content, detritus, has a high specific gravity and tends to fall towards the most declivous part of the ureter. When the detritus is packed just above the stone to form a plug, it effectively prevents the urinary flow and thus causes colic. A plug above a ureteric calculus prevents the contrast medium from reaching the level of the stone and a defect in the contrast medium column will occur just above it (Fig. 1). With a change in position of the patient, the medium may reach the concretion (HOLMLUND 1968).

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Fig 1 Stone in the upper part of the ureter and a contrast filling defect just above the stone

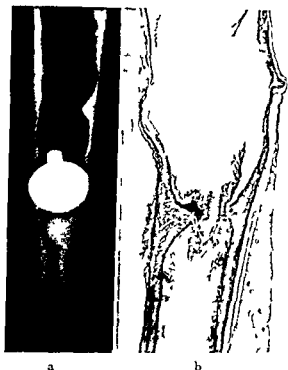


Fig 2 Stone in upper part of the ureter and a filling defect immediately below the stone

*Contrast medium defects just below a ureteric calculus* Experimental studies in rabbits have indicated that the ureteric mucosa below a stone becomes folded when the stone is pressed downwards by increased pressure of urine from above (HOLMUND 1968). An intense inflammatory reaction occurs in the folded mucosa (Fig 3) the inflamed bar preventing the passage of the stone. In human ureters, corresponding changes ahead of a stone may also be verified at ureterolithotomy. Roentgenologically, a bar below a ureteric calculus may be represented by a defect in the contrast medium column just below the stone (Fig 2) (HOLMUND 1968).

*Material and Methods* The routine urographic examinations of 1066 consecutive patients treated during the period 1961–1968 for ureteric stone were investigated for contrast medium defects immediately above and below the calculus. About 20 to 40 ml Urografin 60 % were injected intravenously during one minute. Exposures were made at 3, 10, 15 and 60 minutes, and when necessary at 2 and 4 hours. Sometimes, even later exposures were made.

Fig 3 a) Microradiogram of the ureter of a rabbit in which an artificial concretion was arrested for 24 hours. A bar and a swelling of the ureteric wall can be seen below the concretion. b) Histologic section of the ureteric wall at the level of the stone. The bar was formed by folding of the mucosal and submucosal layers.



In 66 patients, no contrast medium was excreted from the affected kidney, and these patients were excluded from the series.

In 316 patients, no contrast medium was demonstrated in the ureter distal to the stone level, and these were included in the series. Two or more stones were seen in the same ureter in 12 patients, and stones were present in both ureters in 8 patients, in these cases consideration was given to the calculus that was probably causing the acute symptoms of the patient.

A contrast medium defect just above the calculus was registered when two films exposed in the same position of the patient indicated good excretion into the renal pelvis and upper part of the ureter but no medium was seen immediately above the level of the stone.

A contrast medium defect just below the calculus was registered when a narrow and irregular contrast column, or no filling, was observed just below the stone in two or more urograms, with good filling of the remainder of the ureter below it.

The size and position of the ureteric calculi in 1000 patients with acute ureterolithiasis appear in Table 1 and the results of the investigation of contrast medium defects above and, respectively, below the ureteric calculi in relation to position and size are recorded in Tables 2 and 3.

Table 1

*Size and position of the calculi in 1 000 patients with acute ureterolithiasis*

| Size of the stone* | Upper part of ureter | Middle part of ureter | Lower part of ureter | Total |
|--------------------|----------------------|-----------------------|----------------------|-------|
| < 4 mm             | 97                   | 28                    | 560                  | 685   |
| 4-6 mm             | 75                   | 21                    | 143                  | 239   |
| > 6 mm             | 41                   | 12                    | 23                   | 65    |
|                    | 213                  | 61                    | 726                  | 1 000 |

\* Taken as the smallest cross diameter measured directly on the roentgen film without correction for the magnification factor

### Discussion

A defect in the urographic contrast column just above the ureteric concretion was observed in 23 % of the patients. The series was examined according to a common routine and a similar frequency of this roentgenologic sign ought therefore to occur in other clinics. However, little concerning it can be found in the literature. EMMET (1964) mentioned briefly that the contrast medium sometimes seems to end abruptly a few millimetres above the stone but assumed incorrectly (KILL 1957) that in these patients the ureter must have become spastic in the region of the stone. In no other handbook of roentgenology is the sign mentioned, nor have we found it described in any other publication. Emergency urographic examinations in patients with ureteric calculi are sometimes performed in restless patients with severe pain and retained bowel contents and with incomplete or delayed excretion from the affected kidney. Under such circumstances the defect may easily be overlooked.

A defect in the urographic contrast column demonstrated just above the calculus indicates the presence of a detritus plug reducing the urinary flow and thus causing colic. Films with the patient in different positions will reveal when this detritus plug leaves the region of the stone. This may afford valuable guidance to the clinician for treatment of the patient by indicating the best position that will relieve the colic.

Oedema of the ureteric wall at the level of the stone is often noticed at ureterolithotomy. The roentgenologic sign of this oedema, a defect in the contrast

column just below a ureteric calculus but he incorrectly suggested that this defect was due to spasm of the ureter at the level of the stone.



Table 2

*Defects in the contrast medium just above and below a ureterical stone in relation to its position*

| Position of the stone | Defect just above the stone | Percentage | Defect just below the stone | Percentage |
|-----------------------|-----------------------------|------------|-----------------------------|------------|
| Upper part of ureter  | 79                          | 37.1       | 54                          | 25.4       |
| Middle part of ureter | 21                          | 31.4       | 15                          | 24.6       |
| Lower part of ureter  | 123                         | 16.9       | 29                          | 4.0        |
|                       | 223                         | 22.3       | 98                          | 9.8        |

Table 3

*Defects in the contrast medium just above and below a ureterical stone in relation to its size*

| Size of the stone | Defect just above the stone | Percentage | Defect just below the stone | Percentage |
|-------------------|-----------------------------|------------|-----------------------------|------------|
| < 4 mm            | 120                         | 17.5       | 39                          | 5.7        |
| 4-6 mm            | 72                          | 30.1       | 42                          | 17.6       |
| > 6 mm            | 31                          | 40.8       | 17                          | 22.4       |
|                   | 223                         | 22.3       | 98                          | 9.8        |

Deformation of the urinary bladder due to oedema of the interureteric ridge has been described in patients with a stone close to the ureteric ostium (EDLING 1948, WISOFF *et coll.* 1961 and CAMIEL 1962). CAMIEL assumed that a similar oedema at the level of the stone ought also to occur in patients with a calculus in other parts of the ureter but he presented no roentgenologic evidence of such oedema.

The roentgenologic demonstration of an oedematous mucosal bar ahead of a ureteric stone may give the clinician some guidance as to treatment. A concretion cannot pass a large bar in a short time, and if a patient so affected has repeated periods of colic the bar will increase with every period. Ureterolithotomy has to be performed in many of these patients. Transureteral extraction cannot be recommended for two reasons: first because the bar effectively prevents the passing of the stone-extracting device, and secondly because traction of the stone may cause further folding of the mucosa ahead of the stone, and avulsion of the mucosa will occur if the degree of traction increases.

The size of the mucosal bar below a ureteric stone depends on the amount and duration of the force that drives the concretion downwards (HOLMLUND 1968).



Fig 4 Stone in the lower part of the ureter and a filling defect just above the stone



Fig 5 Stone in the lower part of the ureter (arrow) and a filling defect just below the stone

Large calculi are usually lodged in the ureter for a long time and the pressure required to push these downwards must be considerable. The mucosal bar ahead of such a stone becomes of some size and can more easily be verified as a defect in the contrast medium just below the stone than a lesser bar ahead of a small concretion. This corresponds well with the findings that such a defect was verified in 22.5% of our patients with a calculus measuring from 6 mm or more but only in 5.7% of patients with a calculus less than 4 mm in diameter.

Table 2

*Defects in the contrast medium just above and below a ureteric stone in relation to its position*

| Position of the stone | Defect just above the stone | Percentage | Defect just below the stone | Percentage |
|-----------------------|-----------------------------|------------|-----------------------------|------------|
| Upper part of ureter  | 79                          | 37.1       | 54                          | 25.4       |
| Middle part of ureter | 21                          | 34.4       | 15                          | 24.6       |
| Lower part of ureter  | 123                         | 16.9       | 29                          | 1.0        |
|                       | 223                         | 22.3       | 98                          | 9.8        |

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|                   | 223                         | 22.3       | 98                          | 9.8        |

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The size of the mucosal bar below a ureteric stone depends on the amount and duration of the force that drives the concretion downwards (HOLMLUND 1968).



Fig 4 Stone in the lower part of the ureter and a filling defect just above the stone



Fig 5 Stone in the lower part of the ureter (arrow) and a filling defect just below the stone

Large calculi are usually lodged in the ureter for a long time and the pressure required to push these downwards must be considerable. The mucosal bar ahead of such a stone becomes of some size and can more easily be verified as a defect in the contrast medium just below the stone than a lesser bar ahead of a small concretion. This corresponds well with the findings that such a defect was verified in 22.5% of our patients with a calculus measuring from 6 mm or more but only in 5.7% of patients with a calculus less than 4 mm in diameter.

## SUMMARY

Urographies from 1 000 patients with ureteric stones were examined for contrast filling defects above and just below the stone. A defect was present just above the stone in 22.3 per cent of the patients and just below it in 9.8 per cent of the patients. The organic basis and clinical importance of these roentgenologic signs are discussed.

## ZUSAMMENFASSUNG

Die Urographien von 1 000 Patienten mit Steinen im Ureter wurden auf Füllungsdefekte des Kontrastmittels über und unmittelbar unter dem Stein untersucht. Ein Füllungsdefekt war in 22.3 Prozent der Patienten gerade oberhalb des Steines und in 9.8 Prozent gerade unterhalb des Steines vorhanden. Die organische Ursache und die klinische Bedeutung dieser Röntgenzeichen werden diskutiert.

## RÉSUMÉ

Les auteurs ont examiné les urographies de 1 000 malades atteints de lithiase urétérale pour rechercher des images claires dans le moyen de contraste au dessus et juste au dessous du calcul. Il y avait une image claire juste au dessus du calcul chez 22.3 pour cent des malades et juste au dessous chez 9.8 pour cent des malades. Les auteurs étudient la base organique et l'intérêt clinique de ces signes radiologiques.

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## REPEAT DIRECT PYELOGRAPHY VIA NEEDLE NEPHROSTOMY

by

R. VELA NAVARRETE

Percutaneous direct pyelography (antegrade pyelography) has been recommended for diagnostic purposes in cases in which contrast examination of the renal pelvis and ureter cannot be accomplished either by urography or retrograde pyelography (WICKBOM 1954, WEENS & FLORENCE 1954, GOODWIN et coll 1955). Its usefulness has also been suggested in bilateral congenital hydronephrosis when the infant is too small or too frail to withstand cystoscopic manipulations (GOODWIN et coll 1955).

Percutaneous pyelography has been employed by the author in cases in which the pyeloureteric morphology was not disclosed by infusion urography or retrograde techniques. The most frequent indications for its use have been the following: stenosing tuberculous ureteritis, anuria, hydronephrosis or renal

obstruction, ureteroneocystostomy

In addition to these indications recommended by other authors (GOODWIN 1964, MALDONADO 1966), antegrade pyelography has proved useful in selected cases of severe hydronephrosis when the conventional techniques (urography,

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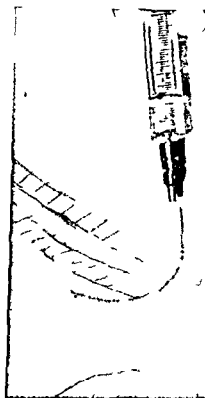


Fig 1 Final position of the catheter after percutaneous puncture of the renal pelvis

isotope examination of renal function and retrograde pyelography) do not offer precise information as to the recuperability of the obstructed kidney. A small plastic tube has been introduced through the needle and left in place as long as necessary in such cases. Three different kinds of studies can be made by means of this nephrostomy (Fig 1): determination of the intrapelvic pressure at rest and immediately after stress hydration (1), permanent divided renal function studies (2), and repeat pyelography in order to follow up the result of drainage (3).

These parameters appear even more valuable when the insufficiency of the classical methods of renal function evaluation are considered (EARLAM 1967). The absence of definition of a hydronephrotic renal pelvis in the urogram does not necessarily mean a low level of function (BRUNSWIG et coll 1964). Reduction in the renal parenchyma, as estimated by measuring the width between the calyces and between them and the cortical margin, need not imply a reduction in renal volume, a significant decrease in thickness is, in fact, compensated for by only a moderate increase in the width of the kidney (EDHOLM & LINDBLOM 1962). A flat, non-functioning curve in the renogram may simply indicate the persistence of obstruction longer than 72 hours, a state that may be reversible upon relief of the obstruction (SMITH & SMITH 1968).

Much information can be determined regarding the recuperability of renal function by following the morphologic changes in the renal calyces and pelvis after the drainage through the plastic tube has been accomplished. Percutaneous pyelography may thus provide information not only of diagnostic value but with prognostic implications as well.

**Technique** There is no substantial difference between our technique of percutaneous pyelography and those previously reported (WICKBOM 1954, GOODWIN et coll 1955). The kidney is delineated with preliminary films. The patient lies in the prone position and percutaneous puncture is made under local anesthesia.

The Vim Silverman standard biopsy needle with the largest plastic catheter that will fit the needle are used. The needle is advanced while the patient holds his breath, and the catheter is passed immediately after the pelvis has been punctured. Fluoroscopy may be necessary in order to leave the tip of the tube in the desired position. Once the tube has been fixed to the skin, the patient is turned supine and 20 to 30 ml of urine are aspirated and 15 to 20 ml of contrast medium are injected during fluoroscopy. Films are obtained in anterior and oblique positions, and with the patient upright. Late films are added if necessary.

The tube is left in situ long enough for sufficient morphologic and functional information to be obtained, during this time antibiotics are introduced through the tube.

The procedure has been well tolerated and the patients do not complain of discomfort. Fever occurred in one patient but was effectively treated with antibiotics. The tube slipped out on two occasions but was easily replaced each time. The injection of contrast medium and the radiographic studies may be repeated as desired.

## Results

Fifteen cases were examined. In 2 cases, the tube was removed during the first 48 hours once the exact diagnostic and prognostic evaluations were made. Only in 4 cases was the tube maintained in position longer than one week.

Sequential events in one case of congenital hydronephrosis are presented in Fig 2. The pyelocalyceal morphology on the first day is depicted in Fig 2a. Films taken on the fifth, tenth and fifteenth days appear in Fig 2b, c and d. Morphologic changes are clearly demonstrated. The decrease in pyelocalyceal distension after the fifteenth day of drainage is remarkable. Twenty two days after the tube was inserted, the patient was operated upon and pyeloplasty performed.

The following features have been considered in the morphologic evaluation



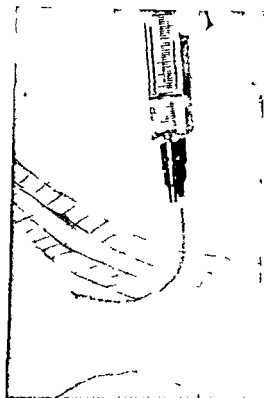


Fig 1 Final position of the catheter after percutaneous puncture of the renal pelvis

isotope examination of renal function and retrograde pyelography) do not offer precise information as to the recuperability of the obstructed kidney. A small plastic tube has been introduced through the needle and left in place as long as necessary in such cases. Three different kinds of studies can be made by means of this nephrostomy (Fig 1): determination of the intrapelvic pressure at rest and immediately after stress hydration (1), permanent divided renal function studies (2), and repeat pyelography in order to follow up the result of drainage (3).

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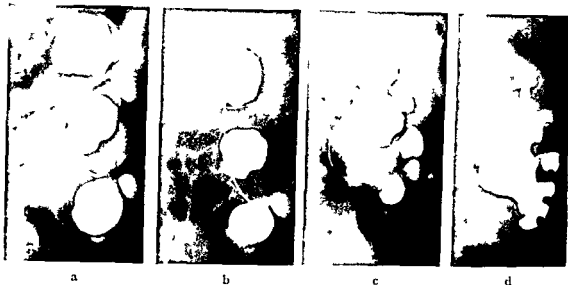


Fig 2 Morphologic changes in a case of hydronephrosis after percutaneous drainage had been established. Films taken on the first, fifth, tenth and fifteenth days respectively.

of a hydronephrotic kidney. 1) Renal size, pyelocalyceal distension, pelvic area and parenchyma thickness are recorded for baseline purposes in the first day study. 2) Films with the patient upright have been especially useful. Even when the functions is fairly good, the intracalyceal residual urine may be detrimental to the kidney. Its persistence during the following days favours extirpative surgery. 3) Repeat pyelography is utilized to follow the sequential changes in the pyelocalyceal morphology. This is important not only in the decision to perform conservative or ablative surgery but it may provide information as to the type of plastic procedure to be done.

### Comments

The method described is especially recommended in cases of chronic, gross hydronephrosis in which the recuperability of the kidney is questionable. These cases present the following features: non-filling of the kidney in the urogram, a curve indicating non-function in the isotope renogram, and marked hydronephrosis with a significant reduction in the renal parenchyma in the retrograde or the direct pyelogram.

The method is simple and no complications have been observed. The patients tolerated the temporary nephrostomy well, which allowed for three different kinds of studies to be made: determination of the intrapelvic pressure, divided renal function studies and repeat percutaneous pyelography.

A progressive decrease in pyelocalyceal distension is considered a favourable sign. Based on the information afforded by this method, a more accurate decision can be made regarding the choice between extirpative or reconstructive surgery. Furthermore, in cases of conservative surgery, the technique may provide information as to the most effective procedure to be selected.

## SUMMARY

Pyelography through a plastic tube introduced into the renal pelvis by percutaneous puncture is described. The procedure enables determination of the intrapelvic pressure, permanent divided renal function studies and repeat pyelography to be made. The indications, procedure, results and prognostic implications are discussed.

## ZUSAMMENFASSUNG

Pyelographie durch eine mittels perkutaner Punktion im Nierenbecken eingeführte Plastikröhre wird beschrieben. Mit dieser Technik ist es möglich den Druck im Becken zu messen, fortlaufende Funktionsstudien der Nieren zu machen und die Pyelographie zu wiederholen. Indikationen, Technik, Resultate und Prognose werden besprochen.

## RÉSUMÉ

L'auteur décrit la pyélographie par un tube plastique introduit dans le bassinet renal par ponction percutanée. Cette technique permet de mesurer la pression dans le bassinet et permet de faire des études permanentes des fonctions de chaque rein isolément et de répéter la pyélographie. L'auteur examine les indications, la technique, les résultats et les conséquences pronostiques de cet examen.

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## ARTERIOVENOUS FISTULAE FOLLOWING PERCUTANEOUS RENAL BIOPSY

by

LEIF EKLUND and TORE LINDHOLM

Arteriovenous fistulae resulting from renal biopsy are presumed to be uncommon. Since the first cases were described in 1962 (BOIJSEN & KOHLER 1962, FERNSTROM & LINDBLOM 1962) further reports of this complication have appeared (ALWALL 1963, BLAKE *et coll* 1963, BENNETT & WIENER 1965, KAUFMAN *et coll* 1965, RUFFY 1965, NILSSON & ROSS 1967, CURRAN *et coll* 1967, FAUST 1968, OCHSNER & BUSCH 1969). The largest clinical material was presented by BENNETT & WIENER (1965), who reported 9 arteriovenous fistulae and 2 arterial aneurysms among 58 patients in whom renal biopsy had been performed. The total number of published cases of fistulae following renal biopsy now amounts to some 30. Experimental investigations in rabbits have indicated that the condition is easily produced by renal biopsy (EKLUND 1970). The present work was intended to investigate angiographically the frequency of such fistulae in patients who had, as well as in those who had not, been previously examined by percutaneous renal biopsy. Some of the angiographies were performed in a current program in which patients are examined both before and after renal biopsy. The examinations followed up in this program are still few in number and will be reported later.



Fig 1 The position of the seven arteriovenous fistulae after right renal biopsy in the present series

*Material and Methods* A total of 1464 nephroangiographies and 601 percutaneous renal biopsies were performed during the period May 1965 to October 1969. Eight of the angiography patients developed arteriovenous fistulae. Seven of these 8 patients had prior to the angiography been examined by percutaneous renal biopsy. The eighth patient, who had not been examined by percutaneous renal biopsy, was a 66 year old man with proteinuria. Angiography had revealed a possible renal cyst which led to thin needle puncture, and further angiography demonstrated a renal fistula. The patient proved to have renal carcinoma. The possibility that the puncture needle damaged tumour vessels cannot thus be eliminated. A traumatising factor could therefore be traced in all these patients and no fistula in the material could be said to be congenital or to have arisen spontaneously.

All the details of angiographies performed following percutaneous renal biopsy as well as the clinical data on the patients have been examined to determine the possible cause for an arteriovenous fistula. The technique of renal biopsy has been described previously (LINDHOLM *et coll* 1967). The angiographies were performed by percutaneous catheterisation of the renal artery from the femoral artery with a radiopaque red thin walled catheter, outer diameter 2.2 mm, inner diameter 1.45 mm. A higher number of films per second than normal was used in large fistulae with early shunting to the veins.

The material comprised 48 biopsies performed in 41 patients, one of whom was examined on three occasions, 5 on two occasions and the rest on one occasion. Of the 7 patients with a renal arteriovenous fistula 4 were women and 3 were men. Of the remaining 34 patients 14 were women and 20 were men.

Table

*Clinical data on seven patients with renal arteriovenous fistula following renal biopsy*

| Case | Age (years) | Days between biopsy and angiography | Blood pressure | Renal bruit | Diagnosis                        | Comments   |
|------|-------------|-------------------------------------|----------------|-------------|----------------------------------|--|
| 1    | 50          | 9                                   | 155/105        | +           | No abnormality                   | Probable pyelonephritis at angiography 4 years after biopsy the fistula had closed         |
| 2    | 22          | 7                                   | 150/100        | ?           | Pyelonephritis                   | The fistula had closed 18 months after biopsy  |
| 3    | 24          | 5                                   | 135/75         | +           | Proliferative glomerulonephritis | The fistula had closed 15 months after biopsy  |
| 4    | 28          | 10                                  | 160/110        | +           | Proliferative glomerulonephritis | Renal bruit disappeared 17 days after biopsy the fistula had closed 16 months after biopsy |
| 5    | 30          | 389                                 | 180/110        | +           | Interstitial nephritis           | Renal resection performed 15 months after biopsy   |
| 6    | 21          | 202                                 | 100/70         | ?           | Amyloidosis                      | The fistula had closed 17 months after biopsy  |
| 7    | 17          | 31                                  | 120/80         | +           | Acute glomerulonephritis         | Biopsy specimen insufficient for diagnosis, the fistula still open 4 months after biopsy   |

The average age of the patients with a fistula was 27.4 years (range 17 to 50 years) and of the remaining patients was 33.0 years (range 13 to 73 years)

The renal blood flow was measured with the dye dilution technique in 3 patients (GOTTLIN & OLIN 1970)

## Results

The frequency of arteriovenous fistula in patients examined by renal biopsy was significantly different ( $p < 0.001$ ) from that in the remainder. The fistulae in all 7 patients moreover occurred in the right kidney — the one on which the biopsy had been performed (Fig. 1) — and the probability of the procedure having been the cause in the 7 patients was obvious.

The interval between the percutaneous renal biopsy and the angiography in the 7 patients averaged  $93 \pm 56$  days (range 5 to 389 days (13 months))



Fig 2 Case 1 Right selective nephroangiography 9 days after biopsy. Fistula at inferior pole with good contrast filling of the inferior branch of the renal vein.

(see Table), while the corresponding interval for the remaining patients was  $430 \pm 61$  days (range 3 to 1368 days (45 months)). The difference between these intervals was significant ( $p < 0.05$ ). In all, there were 14 cases in whom the interval between the renal biopsy and angiography was a month or less. Fistulae were observed in 5 (36%) of these 14 cases while in the 34 cases in whom the interval was longer than a month only 2 had fistulae (6%). The difference between these frequencies was significant ( $p < 0.05$ ).

Arterial blood pressures of 150/100 or higher were recorded in a total of 11 patients 4 of whom (36%) belonged to the group with fistulae. Only 3 (8%) of the remaining 37 cases had a fistula. The difference between these frequencies however, was not significant. Both the systolic and diastolic blood pressures prior to the renal biopsy were unchanged a week later in the 7 patients with fistulae.

Nephrosclerotic vessel changes were observed in 8 of the renal biopsies. Three (38%) of these occurred in patients in the group with fistulae. Four (10%)





Fig 3 Case 3 a) Right selective nephroangiography 5 days after biopsy. Fistula at inferior pole with early filling of veins b) Fifteen months after biopsy, the fistula has closed

of the remaining 40 cases without such vessel changes, had a fistula. The difference between these frequencies was not significant.

Gross hematuria appeared in connection with the renal biopsy in 2 (4%) of the 48 examinations, 1 of these patients had a fistula at subsequent angiography. Perirenal hematoma was also recorded in 2 patients, 1 of whom had a fistula and one had no.

There were no significant differences in the distribution of renal diagnoses between the group of patients with fistulae and the other group.

### Case reports

*Case 1* Woman, aged 50, who for a few years had suffered from bouts of infection of the urinary tract, for which she received antibiotics, was admitted with possible pyelonephritis. A moderate rise in blood pressure (155/105) was recorded but there were no hypertensive changes in the fundi. Urography revealed slight dilatation of the right renal pelvis but otherwise normal conditions. Biopsy of the right kidney yielded a satisfactory quantity of normal tissue.

Angiography demonstrated an arteriovenous fistula at the inferior pole of the right kidney (Fig 2). The examination was first made 9 days after the renal biopsy, control examination 6 days later indicated unchanged conditions. Further angiography about 4 years later demonstrated that the fistula had closed.



a

b

Fig. 1. 18 months after biopsy the fistula has closed

*Case 2* Woman aged 23 who for two years had had symptoms suggesting urinary tract infection. Right renal biopsy indicated pyelonephritis. The clinical details of this case will be published by ALWALL (1970).

Nephroangiography seven days after the biopsy revealed an arteriovenous fistula positioned centrally in the right kidney. The patient was given a long term course of antibiotics controlled by renewed renal biopsies on two occasions, that indicated regression. In spite of these additional biopsies further angiography 18 months after the first, demonstrated that the fistula had closed.

*Case 3* Man aged 24 who had had repeated attacks of hematuria with traces of proteinuria for five years. Renal function, sedimentation rate and blood pressure were normal. Percutaneous renal biopsy was performed and microscopy suggested a resting condition after a previous focal proliferative glomerulonephritis. Nephroangiography disclosed an arteriovenous fistula at the inferior pole of the right kidney with rapid contrast filling of the venous system. This was carried out 5 days after the renal biopsy, further examination 15 months later demonstrated that the fistula had healed (Fig 3, a and b).

*Case 4* Man aged 28 who fifteen years previously had had acute glomerulonephritis that developed after an infected burn. During the years immediately preceding the ex-



Fig 5 Case 5 Right selective nephroangiography 13 months after biopsy. The renal artery is wider than normal. Large arteriovenous fistula in lower part of kidney with early filling of renal veins and inferior vena cava.

amination proteinuria was constant. The blood pressure was 160/110 but the heart size was within normal limits and there was no hypertensive retinopathy. Renal biopsy was performed and microscopy indicated proliferative glomerulonephritis. Signs of nephrosclerosis with thickening of the walls of the vessels in some places was evident. Auscultation over the right kidney five days after the renal biopsy revealed a bruit. Renal angiography 10 days following the biopsy disclosed an arteriovenous fistula at the superior pole of the right kidney (Fig 4a) but auscultation over the right kidney 17 days after the biopsy failed to pick up the bruit. At angiography 16 months later the fistula had closed (Fig 4b).

*Case 5.* Woman, aged 30, with proteinuria 12 years previously, had during the following years been repeatedly treated for a nephrotic syndrome. One year prior to the biopsy the patient was admitted with reduced kidney function and hypertension with blood pressures of the order of 220/130 and hypertensive retinopathy grade IV according to Keith-Wagener. The clinical diagnosis was chronic glomerulonephritis with hypertension and treatment included antihypertensive drugs and azathioprine. When the patient was readmitted the blood pressure was 180/110 and the hypertensive retinopathy had regressed to grade II—III ac-



Fig 6 Case 6 Right selective nephroangiography 7 months after biopsy. Two small aneurysms filled from the ventral artery with immediate filling of the vein draining the lower pole of the kidney.



Fig 7 Case 7 Selective nephroangiography 7 months after biopsy. A large aneurysm filled from the ventral artery with immediate filling of the vein draining the lower pole of the kidney.

According to Keith-Wagener, endogenous creatinine clearance was 32 ml per minute. Following percutaneous renal biopsy the patient developed a perirenal hematoma.

Pathologic examination of the kidney confirmed the earlier biopsy diagnosis of nephrosclerosis and interstitial nephritis. There was, however, no improvement in renal function after the operation.

**Case 6** Woman, aged 21, with rheumatoid arthritis for 5 years was admitted for investigation of an increasing nephrotic syndrome of six months duration. Biopsies from both rectal mucosa and kidney disclosed amyloidosis. Right selective nephroangiography about 7 months later demonstrated two small aneurysms that filled from the peripheral branches of

the ventral artery with immediate filling of the veins draining the caudal part of the kidney (Fig 6) The blood flow through the arteriovenous fistula was estimated to be 3 % of the total blood flow to the kidney Further angiography about 17 months later revealed closure of the fistula

*Case 7* Boy, aged 17, who five months prior to the examination developed lumbar pain and hematuria after a throat infection Only traces of proteinuria were present and the sedimentation rate, serum electrophoresis and blood pressure were all normal, the anti streptolysin titer, however, was increased and the condition was clinically designated as acute glomerulonephritis Renal biopsy was performed but the material obtained was insufficient for a diagnosis Following the renal biopsy the patient developed temporary gross hematuria

Nephroangiography 31 days after the renal biopsy revealed an arteriovenous fistula in the dorsal artery of the right kidney (Fig 7) The blood flow through the fistula was estimated to be 54 % of the total blood flow to the kidney Further renal angiography 3 months later indicated that the arteriovenous fistula was still there

### Discussion

Renal arteriovenous fistulae arising after renal biopsy have a tendency to spontaneous healing, which was recorded in 5 of the 7 patients of the present material at repeat angiographies Spontaneous healing of similar fistulae has also been observed previously in a clinical material by BENNETT & WIENER (1965) and NILSSON & ROSS (1967) as well as in an experimental project by EKLUND (1970) This tendency to spontaneous healing ought to explain why the frequency of arteriovenous fistulae was significantly higher if the interval between the percutaneous renal biopsy and the renal angiography was one month or less than if the same interval was longer

The risk of an arteriovenous fistula arising after percutaneous renal biopsy is reported to be greater if the patient has hypertension and nephrosclerosis (BOIJSEN & KOHLER 1962, BLAKE et coll 1963) In the present series 11 patients had a blood pressure of 150/100 or higher Of these 36 % developed fistulae, while the corresponding figure for the patients with a lower blood pressure was 8 % Nephrosclerotic vessel changes were recorded in the kidney preparations from 8 patients, 38 % of whom developed arteriovenous fistulae Fistulae appeared in only 10 % of the remaining 40 cases These percentages appear to indicate the risk of the fistulae being increased with hypertension and nephrosclerosis, but it should be noted that in neither case was the difference statistically significant, and that the material was small There was no correlation between the appearance of the fistulae and other complications associated with renal biopsy, such as gross hematuria and hematoma formation

The renal tissue distal to a fistula may have a reduced blood supply which could activate renin production and cause hypertension (MILLOI et coll 1958)

On the other hand, a reduction in the blood pressure probably due to gross shunting through a fistula has also been reported (NILSSON & ROSS 1967). No significant change in blood pressure was noted in any of the patients of the present material.

Only a few major series of renal angiographies of patients examined by renal biopsy have previously been reported. FERNSTROM & LINDBLOM (1962) described a patient with a fistula following renal biopsy and afterwards examined a further 20 patients without discovering another fistula. BENNETT & WIENER (1965) examined 58 hypertensive patients by renal angiography following renal biopsy and recorded arteriovenous fistulae in 9 (16%) of them. This frequency is close to that in the present series of 48 examinations in which arteriovenous fistulae were noted in 7 (15%) of the patients. All 7 fistulae were situated centrally in the kidney. FAUST (1968) pointed to arteriovenous fistulae after renal biopsy.

renal biopsies should if possible be done cortically

## SUMMARY

Nephroangiography was performed in 41 patients examined by percutaneous renal biopsy on 48 occasions. Arteriovenous fistulae occurred in 7 (15 per cent) of the patients. Spontaneous closure of the fistulae was demonstrated in 5 of the patients. Hypertension and nephrosclerosis seemed to increase somewhat the risk of a fistula formation following the biopsy.

## ZUSAMMENFASSUNG

Nephroangiographie wurde an 41 Patienten vorgenommen bei denen 48 Nadelbiopsien vorher ausgeführt worden waren. In 7 (15 Prozent) der Patienten konnte eine arteriovenöse Fistel aufgezeigt werden. In 5 Patienten erfolgte später eine spontane Heilung der Fisteln. Es scheint, dass sowohl der Hochdruck als auch das Bestehen einer Nephrosklerose das Risiko einer arteriovenösen Fistelbildung fordert.

## RÉSUMÉ

Les auteurs ont fait des angiographies rénales chez 41 malades qui avaient eu 48 biopsies rénales percutanées. Ils ont trouvé des fistules artério-veineuses chez 7 de ces malades (15%). Ils ont mis en évidence la fermeture spontanée de la fistule chez 5 de leurs malades. L'hypertension et la néphro-sclérose paraissent augmenter un peu le danger de formation d'une fistule après la biopsie.

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## SUMMARY

Nephroangiography was performed in 41 patients examined by percutaneous renal biopsy on 48 occasions. Arteriovenous fistulae occurred in 7 (15 per cent) of the patients. Spontaneous closure of the fistulae was demonstrated in 5 of the patients. Hypertension and nephrosclerosis seemed to increase somewhat the risk of a fistula formation following the biopsy.

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## ANGIOGRAPHY IN JUXTACORTICAL OSTEOSARCOMAS

Case report with special reference to the differential diagnosis

by

FRANZ P PROBST

Juxtacortical osteosarcomas (synonyms parosteal osteogenic sarcomas, ossifying parosteal sarcomas, parosteal and periosteal ossifying fibrosarcomas) have typical histologic appearances and run a characteristic clinical course. They are of low malignancy and thus differ unmistakably from, for instance, osteoblastic osteogenic sarcomas. Roentgenologically however, certain difficulties are encountered in their differentiation. It may be of interest to describe a case in which arteriography was carried out, seeing that examination of the blood vessels has been reported in only one other similar case (LAGERGREN et coll 1961), and also because angiography appears to assist in the differential diagnosis.

### Case report

A man aged 24 had for six months noticed a hard slow-growing lump distally in the left thigh but had no other symptoms. Conventional roentgen examination (Fig 1 a and b) revealed a large irregularly shaped highly sclerotic bony mass which surrounded the femur without appearing to affect the cortex. Angiography (Fig 1, c and d) disclosed local displacement of the popliteal artery and a few small arterial branches but no blood vessels

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Fig 1 Juxtacortical osteosarcoma: a) and b) Densely ossified broad based mass surrounding the posterior medial and anterior aspects of the distal part of the femur. Thin soft tissue interposition between cortex and tumour best seen in the oblique view (b) Femoral angiography arterial phase c) Frontal and d) oblique views. Popliteal artery displaced laterally by tumour with all contiguous arteries also stretched and displaced around surface of the growth. No intratumoural vessels filled. Tumour lacks angiographic signs of malignancy.



Fig 2 Same case as in fig 1 after incomplete local excision. Conventional lateral view (a). Femoral angiography six months after operation, arterial phase, frontal (b) and lateral (c) views. Medial popliteal branch and descending branch from femoral artery now absent. Displacement of remaining arteries no longer present. Still no pathologic vascularization of remaining part of tumour.



Fig 3 Same case as in figs 1 and 2 eighteen months after operation. Tumour about the same size as before the operation but more densely calcified.

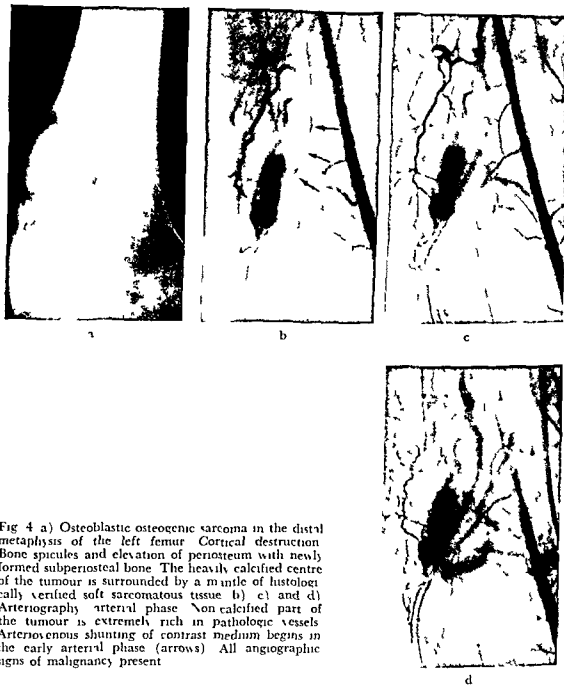


Fig 4 a) Osteoblastic osteogenic sarcoma in the distal metaphysis of the left femur. Cortical destruction. Bone spicules and elevation of periosteum with newly formed subperiosteal bone. The heavily calcified centre of the tumour is surrounded by a mantle of histologically verified soft sarcomatous tissue. b) c) and d) Arteriography, arterial phase. Non calcified part of the tumour is extremely rich in pathologic vessels. Arteriovenous shunting of contrast medium begins in the early arterial phase (arrows). All angiographic signs of malignancy present.

were distinguishable within the tumour itself. The patient refused amputation but agreed to local excision (Fig 2 a). Histopathologic diagnosis: juxtacortical osteosarcoma. Angiography (Fig 2 b and c) six months later: filled no blood vessels in the remaining parts of the tumour. The patient has been followed up during the eighteen months that have passed since the operation and the tumour is still growing slowly (Fig 3). There have been no signs of metastases.



Fig 5 Osteoblastic osteogenic sarcoma of left os calcis a) and b) Conventional roentgenograms Bone structure appears preserved (note apparently normal trabeculation) but neoplastic bone with extensive fine spicules outside the ordinary border A thin soft tissue layer seems to be interposed between the cortex and the extraosseal part of the tumour (arrows)

### Discussion

The most important roentgenologic feature in juxtacortical osteosarcoma is excessive new growth of bone, so that the type of neoplasm can usually be recognized at the conventional roentgen examination Highly osteoblastic osteogenic sarcoma and myositis ossificans may however cause difficulties in the differential diagnosis, in both of these new bone formation dominates the appearances



Fig 6 Same case as in fig 5 Arteriography different stages of arterial phase Subtraction films The tumour is richly vascularized with unequal distribution of vessels Early filling of draining veins (arrows) in (c) and (d)

The intraosseous tumour tissue and cortex destruction are generally so marked in osteoblastic osteogenic sarcoma that there is little likelihood of mistaking them for juxtacortical osteosarcoma, even with conventional roentgenography. The intraosseous involvement may sometimes be less marked, however, and a risk of confusion with juxtacortical osteosarcoma may then arise.

The significance of angiography in the differential diagnosis may be illustrated by 2 cases of verified osteogenic sarcoma in which angiography was also performed. In the first case (Fig. 4), the characteristic features of osteogenic sarcoma were already distinguishable at conventional roentgen examination. Angiography revealed a large number of pathologic blood vessels with the typical indications of malignancy. An osteogenic sarcoma in the other case was located in the calcaneus (Fig. 5). As the site of the tumour was uncommon and the newly formed bone was largely situated near the cortex, it was considered that conventional roentgenography would fail reliably to disclose the type. Angiography revealed pathologic vessels typically associated with a malignant tumour in this case as well (Fig. 6). The circulation speed was rapid but varied in different parts of the tumour, this could be clearly demonstrated with the aid of the multicolour subtraction method (Fig. 7) described by WFLANDER (1969). The angiographic appearances in osteogenic sarcoma have been known for some years (LAGERGRÉN *et coll.* 1961), and angiography would seem to be a valuable differential diagnostic aid where the tumour may be a juxtacortical osteosarcoma.

New bone formation, often extensive, is the dominating feature at the conventional roentgen examination in myositis ossificans and the new bony tissue may be situated in the immediate vicinity of a skeletal bone. Another factor that may complicate the differential diagnosis is that in certain phases of cell-rich proliferation the histologic appearances of the tissue may be mistaken for sarcoma, and this may lead to the performance of mutilating operations. We have performed angiography in a case of myositis ossificans (Fig. 8). A large number of fine blood vessels as well as an accumulation of contrast medium were evident. The vascularity differed widely from the appearances in the case reported of juxtacortical osteosarcoma, in which there was a paucity of blood vessels. On the other hand, the vessels did not look like those commonly seen in malignant tumours for instance in osteogenic sarcomas. Three cases with similar vascular appearances have been described by STFNER & WICKBOM (1966). These proved to be muscle ruptures with organizing haematomas, but without calcifications or new bone formation.

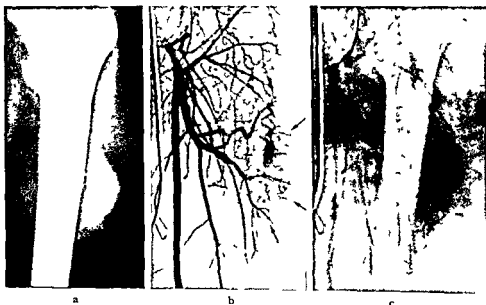
It is of course not possible to base general conclusions on isolated cases. However, the angiographic investigations mentioned in this paper suggest that angiography may be a valuable aid in the diagnosis of juxtacortical osteosarcoma, and



Fig 7 Same case as in figs 5 and 6 Multicolour combination image of three films from the arterial phase taken at an interval of two seconds between single exposures The colour of the vessels yellow, magenta and cyan, indicates filling of the vessels in the different primary film components Rapid circulation through the tumour as well as different parts of the tumour are demonstrated (This multicolour image was prepared by the method described by WELANDER )







a

b

c

femoral region conventional frontal view (a) Mass early (b) and late (c) arterial phase Tumour richly irregular arteries Rapid passage of the contrast medium (arrows) Equal distribution of vessels within the mass

The angiographic appearances may give the impression of malignancy, but differ significantly from those observed in cases of osteoblastic osteogenic sarcoma (cf figs 4 to 7)

for differentiating this form of tumour from other lesions producing similar appearances at conventional roentgenography

## SUMMARY

Angiography has been used in a case of juxtacortical osteosarcoma The value of this method in the differential diagnosis is discussed in the light of the information obtained at angiography of two cases of osteogenic sarcoma and one case of myositis ossificans

## ZUSAMMENFASSUNG

## RÉSUMÉ

L'auteur a fait une angiographie dans un cas d'osteosarcome juxtacortical. Il examine l'intérêt de cette méthode pour le diagnostic différentiel en se basant sur les signes angiographiques obtenus dans deux cas de sarcome ostéogénique et dans un cas de myosite ossifiante.

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## EFFECTS OF SALICYLATES ON THE GASTRIC MUCOSA AS REVEALED BY ROENTGEN EXAMINATION AND THE GASTROCAMERA

by

D EDMAR

A diversity of opinions appears to exist in the literature on the possible effect of acetylsalicylic acid as the cause of acute gastritis, gastric haemorrhage and peptic ulceration. DOUTHWAITE and PAUL may for example be cited as two scientists with diametrically opposed theories. DOUTHWAITE, who together with LINTOTT (1938) was one of the first to use the gastroscopic method in the investigation of the effects of the drug on the gastric mucosa, gave one gram to sixteen patients and after half an hour was able to establish varying degrees of hyperemia, submucous haemorrhage and ulcerative changes in the gastric mucosa in thirteen of the patients. PAUL (1943), on the other hand, reported no such changes in patients with functional or organic gastric disease, after single or repeated doses of acetylsalicylic acid, and therefore considered that in doses as large as 5.33 g daily the drug failed to influence the gastric mucosa, as viewed in the gastroscope. WOLF & WOLFF (1943) could not demonstrate any changes in the gastric mucosa when they tested the effects of the substance in their famous patient with a gastric fistula. Further research, to which I will refer later, and clinical experience (e.g. PARRY & WOOD 1967, VALMAN, PARRY & COGHILL

1968), clearly indicate that acetylsalicylic acid may be a factor in the development of gastritis, ulceration and haemorrhage. The matter is nevertheless still controversial. The reasons for the divergent opinions are probably partly the absence of accurate photographic documentation and partly the lack of comparative control investigations. In many instances, only single doses of the drug were given, and the period during which the gastric mucosa was exposed to the drug was comparatively short.

*Method and Material* An investigation of the effects of two salicylates on the gastric mucosa was performed with the gastroscope as well as with roentgen during a period of three months in 1969. The investigation was not limited to gastric photography since the duodenal bulb cannot be examined with the gastroscope. Roentgen examinations were therefore also carried out, with simultaneous examination of the stomach and duodenum to determine whether gastric changes could be diagnosed also roentgenologically. The gastroscope, an Olympus GT-Va, has been described by PERNA, HONDA & MORRISSEY (1965), GABRIELSSON (1967), SCARROW (1967) and COLCHER (1968), inter alios.

The salicylates used in the investigation were acetylsalicylic acid (Magnecyl, ACO) and salicylsalicylic acid (Nobacid, Bofors Nobel-Pharma). The Magnecyl tablets contain 0.5 g acetylsalicylic acid buffered with 70 mg heavy magnesium oxide. The Nobacid tablets contain 0.5 g salicylsalicylic acid with 72.5 mg heavy magnesium oxide.

Eight male volunteers offered themselves for the investigation. Pre-examinations with a barium meal and a gastroscope were performed. The most suitable dose of active substance was determined to 4 grams, divided into four daily doses of 1 g each over a period of one week. This dosage does not exceed the therapeutically recommended one for treatment of e.g. rheumatic diseases.

The investigation was performed double-blind and cross-over with the use of a placebo. Before changing over to a new preparation, each volunteer was kept without drugs for an interval of 2 weeks. The tablets were not to be taken on an empty stomach, except on the morning of the investigation, to ensure that no food particles remained in the stomach.

On the morning of the examination, 1 g of the active substance was given 2 hours before the test, followed 15 minutes before gastrophotography by 1 mg atropine injected subcutaneously. No other drugs were administered apart from a superficial anaesthetic to the pharynx with a xylocaine or carbocaine spray before the insertion of the camera itself. The stomach was emptied with a tube before each gastrophotography, the contents being examined macroscopically and tested with a Hemastix.

Roentgen examination was performed on the day following gastrophoto

graphy in order to prevent the roentgenograms from being affected by the pre medication and the inflation of the stomach at gastrophotography, before roentgen examination each volunteer therefore took the tablets for one day more than before gastrophotography. The roentgen films were interpreted independently by the author and another experienced roentgenologist, who both at that time were unaware of which substance the volunteers had received, the other examiner had no knowledge of the results of gastrophotography. The interpretations of the films by the two examiners did not differ.

### Results

At the pre examination no abnormality of the stomach was revealed by the barium meal or by gastrophotography.

Enlarged mucosal folds were seen on barium meal examination after the administration of acetylsalicylic acid to three volunteers. In two of the volunteers the mucosal folds were possibly a little more distinct than in the pre-examination.

ologic change appeared after administration of this drug.

No gastric abnormality was seen after placebo.

In the duodenal bulb, no changes could be observed except possibly somewhat prominent folds in one of the subjects after the administration of acetylsalicylic acid.

The results of the barium meal examinations are recorded in Table 1.

On gastrophotography multiple small erosions in the gastric mucosa were observed in all the subjects after the administration of acetylsalicylic acid, in places the gastric mucosa was also hyperemic.

Similar small erosions were observed in one subject after medication with salicylsalicylic acid but only in the upper part of the stomach. A somewhat reddish mucosa was also observed after this drug in one subject while in the remaining six no definite gastric changes were seen. No abnormalities were seen after giving a placebo.

The results of gastrophotography are given in Table 2.

Before administration of the drug the gastric contents were soft and with clots of size 1-2 mm. After administration of the drug the contents of the stomach in all the eight volunteers were soft and with clots of size 1-2 mm. After the administration of salicylsalicylic acid only separate small blood clots could be observed in one subject. No changes in the gastric contents could be seen after placebo administration.

Table 1

*Results from the barium meal examinations in the eight volunteers with reference to the appearance of the gastric mucous membranes\**

|   | Pre-examina-<br>tion | After administration of      |                              |         |
|---|----------------------|------------------------------|------------------------------|---------|
|   |                      | Acetyl-<br>salicylic<br>acid | Salicyl<br>salicylic<br>acid | Placebo |
| No visible changes                                | 8                    | 3                            | 7                            | 8       |
| Possibly somewhat more prominent<br>mucosal folds | —                    | 2                            | 1                            | —       |
| Somewhat thicker folds                            | —                    | 3                            | —                            | —       |

\* No changes were seen in the duodenal bulb, except possibly in one subject, in the form of some what more prominent folds, after the administration of acetylsalicylic acid

Table 2

*Results of gastrophotography in the eight volunteers*

|   | Pre<br>examina<br>tion | After administration of     |                              |         |
|---|------------------------|-----------------------------|------------------------------|---------|
|   |                        | Acetyl<br>salicylic<br>acid | Salicyl<br>salicylic<br>acid | Placebo |
| No visible changes                        | 8                      | —                           | 6                            | 8       |
| Reddish gastric mucosa but<br>no erosions | —                      | —                           | 1                            | —       |
| Multiple erosions                         | —                      | 8                           | 1                            | —       |

A positive Hemastix test on the stomach contents was obtained with +++ in all the eight subjects after the administration of acetylsalicylic acid. After salicylsalicylic acid, the Hemastix test was negative in three subjects, + positive in three, and ++ positive in two subjects.

A positive Hemastix test was obtained after the placebo with +++ in two subjects and + in one subject, probably due to small mucosal lesions in connection with the anaesthesia of the pharynx before the examination. During application of the anaesthesia, coughing and hawking sometimes occurred, and in one subject an obvious small mucosal lesion was present on the soft palate. It is also

Table 3

*Subjective side effects after the administration of acetylsalicylic and salicylsalicylic acids and after placebo in the eight volunteers*

|                              | Acetylsalicylic acid | Salicylsalicylic acid | Placebo |
|------------------------------|----------------------|-----------------------|---------|
| Heartburn                    | 1                    | —                     | —       |
| Slight epigastric discomfort | 2                    | 2                     | —       |
| Tinnitus                     | 2                    | 1                     | —       |
| No adverse symptoms          | 3                    | 5                     | 8       |

possible that a small mucosal lesion may have been caused by the gastric tube when emptying the stomach

Subjective side effects were few and slight (Table 3). No complaints of nausea, vomiting, dizziness, dullness of hearing, headache or perspiration during the drug administrations were recorded. It is notable that three of the eight subjects with gastrophotographically determined multiple gastric erosions after acetylsalicylic acid experienced no discomfort at all.

### Discussion

Gastritis is generally diagnosed roentgenologically by the thickened mucosal folds of the stomach. The diagnosis is however not at all certain as the gastric folds normally vary considerably in thickness depending on the variable tone of the muscle layer of the mucosa and the distention of the stomach. SETÄLÄ & SIITALA (1956) have stated that thick mucosal folds of the stomach generally correspond to histologically demonstrable inflammatory changes in chronic gastritis. Many authors hold the opinion however that the correlation between roentgenologically determined thick mucosal folds and gastroscopic or histologic evidence of gastritis is unsatisfactory. Comparison of the results from roentgen examination and gastrophotography in the present investigation support the latter opinion. In all the eight subjects, multiple erosions were observed with the gastroscope after the administration of acetylsalicylic acid, whereas in the roentgen examination slightly thickened mucosal folds were observed in only three subjects and possibly in two others. The increased thickness of the mucosal folds was however in none of these sufficiently marked to label them as pathologic without consideration of the respective pre-examinations. Compared with the gastrophotographic findings the roentgenologic changes were always small.

As has been shown by EDLUND *et coll.* (1961), local thickening of the mucosal



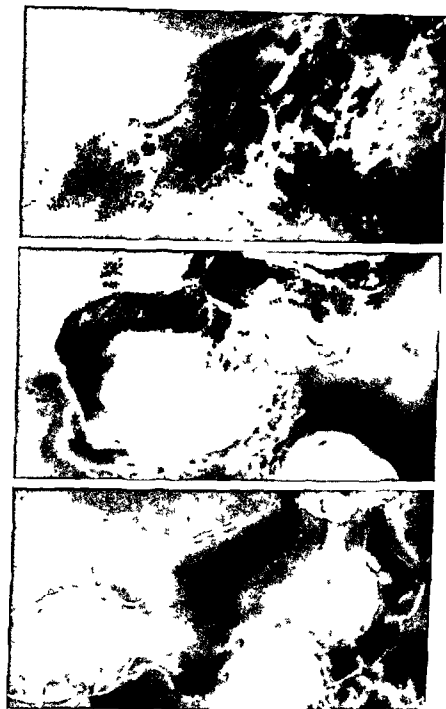


Fig 1 Roentgenograms of the pyloric part of the stomach at the angular notch *Upper* Pre examination No visible changes except for small air bubbles in the pyloric canal *Middle* After acetylsalicylic acid somewhat more prominent mucosal folds compared with the pre examination *Lower* After salicylsalicylic acid no changes in the thickness of the mucosal folds compared with the pre examination



Pre examination Normal gastric mucosa, a peristaltic wave has just passed the proximal part of the antrum, which explains the mucosal folds seen to the left at the bottom of the view

4



After acetylsalicylic acid Multiple erosions of the mucosa in the form of red strings of varying length The dark spot on the left is the pylorus

After salicylsalicylic acid. No visible erosions, thin greyish white coatings are seen in some parts of the mucosa.

Fig 2 Gastrophotographs from the same part of the stomach as in fig 1 The small white dots represent light reflexes

Pre examination Normal mucosa with several slanting mucosal folds (on the right)



After acetylsalicylic acid Multiple erosions with small haemorrhages and blood clots



After salicylsalicylic acid Mucosa as in the pre examination At the top greyish-white coating on the mucosa and further down to the left a smaller but similar coating

Fig 3 Gastrophotographs of the lateral part of the gastric fornix (Roentgen examination of comparative parts of the stomach revealed no changes) The small white points represent light reflexes

folds in one part, e.g. the antrum, as compared with other parts of the stomach, is more diagnostic in the roentgenologic determination of gastritis than generally thickened mucosal folds. Thick mucosal folds limited to certain parts of the stomach were not observed in this investigation, however.

The result of the present study is in agreement with recent investigations in which the gastric mucosa has been examined after the administration of acetyl salicylic acid either in connection with surgery (Muir & Cossar 1955, 1959) or with gastroscopy (Weiss et coll 1961). Vickers & Stanley (1963) presented photographic evidence of gastric mucosal injury in four patients after acetylsalicylic acid. Tjorssen et coll (1968) demonstrated with gastrophotographic methods that hemorrhage, petechiae and echymoses in the gastric mucosa are common in healthy university students with a low gastric pH when this substance has been given. There are many reports in the literature on the occurrence of blood in aspirated gastric juices after the administration of acetylsalicylic acid (Muir & Cossar 1955 and Schneider 1957).

The evidence of gastric mucosal injury by acetylsalicylic acid in the present investigation is clear, since after its administration multiple small gastric erosions appeared in all the eight subjects. Only minor similar erosions occurred in one subject when salicylsalicylic acid had been given. Thus, compared with acetyl salicylic acid, less injury to the gastric mucosa is caused by salicylsalicylic acid. These facts are in accordance with findings in animal investigations (Åberg 1966).

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### SUMMARY

The effects of acetylsalicylic acid and salicylsalicylic acid on the gastric mucosa have been investigated roentgenologically and with the gastroscope in eight volunteers. The administration of acetylsalicylic acid always produced wide spread erosions but only minor similar changes were observed in one subject after salicylsalicylic acid.

### ZUSAMMENFASSUNG

Die Wirkung der Acetylsalicylsäure und Disalicylsäure auf die Magenschleimhaut wurde mit Gastrokamera und Röntgen an acht freiwilligen Versuchspersonen studiert. In sämtlichen Fällen, wo Acetylsalicylsäure gegeben wurde, kam es zu ausgedehnten Erosionen der Magenschleimhaut. Nur in einem Fall waren nach Verabreichung von Disalicylsäure nur geringe Veränderungen zu sehen.

## RÉSUMÉ

L'auteur a étudié sur huit volontaires, par radiographies et par gastrocamera les effets de l'acide acétylsalicylique et de l'acide salicylsalicylique sur la muqueuse gastrique. L'administration d'acide acétylsalicylique a toujours donné lieu à des érosions largement disséminées, mais on n'a constaté de légères lésions semblables après administration d'acide salicylsalicylique que chez un seul sujet.

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## THE ADRENAL GLANDS AFTER EPINEPHRO- PHLEBOGRAPHY

by

C G MIKAELSSON

The introduction of a new investigatory method always raises the question of the risks involved. Epinephro-phlebography described by BUCHT (1962), BUCHT et coll (1964) and MIKAELSSON (1967, 1968, 1969) et alios involves the retrograde injection of contrast medium into the venous system of the adrenal glands through a catheter introduced into the drainage vein. The toxicity and ionic concentration of the contrast medium as well as the increased pressure produced in the venous system during the injection constitute the possible risks, venous rupture within the adrenal gland may occur in extreme cases.

Apart from the clinical examination, the only method of assessing the state of the adrenal glands in situ is to examine the hormonal content of adrenal venous blood samples both before and after artificial stimulation with ACTH.

*Material and Methods* A small series of tests involving sampling both before and just after phlebography was performed in benign essential hypertension to study any possible effects of the contrast examinations on the spontaneous activity of the adrenal glands. The series comprised 5 cases, four of which were examined on the left side and the fifth on the right side. The results are presented in Table 1. Two

Table 1

*The cortisol content of the adrenal veins before and after phlebography with Urografin 76% in five cases*

| Age (years)<br>and sex | Gland | $\mu\text{g}$ cortisol/100 ml plasma |  | Vena cava |
|------------------------|-------|--------------------------------------|--|-----------|
|                        |       | Before phle-<br>bography             | Max. 15 min<br>after phle-<br>bography |           |
| 49 ♂                   | Left  | 2 030.5                              | 914.3                                  | —         |
| 31 ♀                   | Left  | 753.9                                | 488.6                                  | 23.2      |
| 32 ♀                   | Left  | 90                                   | 56.3                                   | 17.4      |
| 32 ♀                   | Left  | 17.1                                 | 32.3                                   | 25        |
| 49 ♀                   | Right | 16.5                                 | 21.3                                   | 16.1      |

similar cases were studied after stimulation with ACTH, of the left gland alone and of both glands, respectively (Table 2)

The analyses of adrenal venous blood from 44 glands in the series of epinephro-phlebographies reported previously (MIKAEELSSON 1969) were also available. No samples in this series were taken before phlebography. The following conditions were represented: aldosteronoma (one gland on the left side), pheochromocytoma (both glands of the same case), pancreatitis (both glands of the same case, one with a small inactive adenoma), hypophysial feminizing adenoma (one gland on the left side), possible adrenal insufficiency (both glands of the same case), benign essential hypertension (thirty-three glands) and malignant essential hypertension (both glands of the same case).

*Sampling* All adrenal venous blood was obtained by spontaneous backflow through the catheter, the external end of which was held about 10 cm above the examination table. The samples were taken immediately before phlebography in 5 cases and immediately after the contrast examination in all cases. The sampling took 1 to 15 minutes. Samples were also usually obtained from the vena cava and were drawn with a syringe after that the adrenal blood had been removed from the catheter.

The position of the catheter was carefully checked before and after sampling, as well as before and after phlebography to ensure that it remained unaltered in position. In the small series (Table 1) the tip of the catheter on the left side lay in the truncus adreno-diaphragmaticus below the inferior phrenic vein without causing occlusion of the former. The non-obstructing position of the catheter is relatively easy to control on the left side but more difficult on the right side. The position just before phlebography was checked by careful injection of a small

Table 2

Adrenal reaction to intravenous administration of ACTH after phlebography with Urografin 76 %

|                        | Time after injection |     | $\mu$ g cortisol/<br>100 ml plasma<br>Left gland | Time after injection |     | $\mu$ g cortisol/<br>100 ml plasma<br>Right gland |
|------------------------|----------------------|-----|--|----------------------|-----|---|
|                        | Min                  | Sec |  | Min                  | Sec |   |
| Case 1                 |                      |     |  |                      |     |   |
| Before Synacten        |                      |     | 457.6  |                      |     |   |
| After 0.25 mg Synacten | 1                    | 5   | 376.8  |                      |     |   |
|                        | 1                    | 40  | 262.2  |                      |     |   |
|                        | 2                    | 10  | 677.8  |                      |     |   |
|                        | 3                    | 10  | 1027.1   |                      |     |   |
|                        | 5                    |     | 1782.9   |                      |     |   |
|                        | 7                    | 30  | 1994.4   |                      |     |   |
|                        | 10                   |     | 2378.7   |                      |     |   |
|                        | 15                   |     | 3332.1   |                      |     |   |
|                        | 20                   |     | 3522.8   |                      |     |   |
|                        | 25                   |     | 3522.8   |                      |     |   |
|                        | 30                   |     | 3713.5   |                      |     |   |
|                        | 35                   |     | 328.9  |                      |     |   |
| Case 2                 |                      |     |  |                      |     |   |
| Before Synacten        |                      |     | 542.8  |                      |     | 493.3   |
| After 0.25 mg Synacten | 15                   |     | 160.1  | 11                   |     | 909.9   |
|                        | 25                   |     | 1735.0   | 25                   |     | 1695.3  |
|                        | 35                   |     | 271.3  |                      |     |   |

Case 1 Man aged 37 years with benign essential hypertension

Case 2 Man aged 52 years with malignant essential hypertension, right gland examined 130 minutes after Synacten administration to left gland

amount of contrast medium, IV screening indicated that this never reached the gland.

The adrenal reaction to stimulation with ACTH after phlebography was studied as follows. After an initial sample, 0.25 mg Synacten was injected into a peripheral vein and repeated samples of adrenal venous blood taken. In the one case, the left gland alone was studied, initially one sample about every minute and then one every fifth minute until the 35th minute were obtained. In the other case, both glands were investigated, each after an individual injection of Synacten, the left about two hours before the right. Technical difficulties limited the number of samples in the latter.

Blood samples were centrifuged and the plasma frozen before transport to the endocrinologic laboratory, where the cortisol content was analysed according to a method described by DE MOORE et coll (1962), modified by LAURELL (un-



Table 3

*Cortisol content in adrenal venous blood maximum 15 minutes after phlebography with Urografin 76 %*

| Case | Age (years)<br>and sex | Diagnosis                        | $\mu\text{g}$ cortisol/100 ml plasma |             |
|------|------------------------|----------------------------------|--------------------------------------|-------------|
|      |                        |                                  | Vena cava                            | Right gland |
| 27   | 56 ♂                   | Benign essential hypertension    | 57                                   | 4 876       |
| 28   | 39 ♀                   | Benign essential hypertension    | —                                    | 3 592*      |
| 17   | 62 ♂                   | Benign essential hypertension    | 19                                   | 1 539       |
|      |                        |                                  |                                      | 2 216       |
| 4    | 30 ♀                   | Benign essential hypertension    | 54                                   | 2 084       |
|      |                        |                                  |                                      | 2 211       |
| 25   | 51 ♂                   | Benign essential hypertension    | 15.5                                 | 2 085       |
|      |                        |                                  |                                      | 422         |
| 21   | 5 ♂                    | Malignant essential hypertension | —                                    | 1 545       |
| 19   | 20 ♂                   | Benign essential hypertension    | 23                                   | 1 393       |
| 18   | 34 ♂                   | Benign essential hypertension    | 29.9                                 | 1 317.6     |
| 14   | 49 ♀                   | Pancreatitis                     | 32                                   | 1 314       |
| 9    | 49 ♂                   | Benign essential hypertension    | 33                                   | 781         |
| 13   | 17 ♀                   | Benign essential hypertension    | 100                                  | 753         |
| 1    | 25 ♀                   | Benign essential hypertension    | 378                                  | 433         |
| 26   | 38 ♀                   | Possible adrenal insufficiency   | 13.9                                 | 404.2       |
| 11   | 32 ♀                   | Benign essential hypertension    | 47.6                                 | 187.6       |
| 22   | 36 ♀                   | Benign essential hypertension    | 35.2                                 | 116.1       |
| 12   | 44 ♂                   | Benign essential hypertension    | 27                                   | 66          |
|      |                        |                                  |                                      | 60          |
| 23   | 37 ♂                   | Phaeochromocytoma                | 22                                   | 51          |
| 24   | 21 ♂                   | Benign essential hypertension    | 20                                   | 21          |
|      |                        |                                  | Mean value                           | 1 248.5     |

\* Intraglandular venous rupture

published) The limits of failure with the method are within  $\pm 10$  per cent. All values in this study are given as the amount of cortisol expressed in  $\mu\text{g}$  per 100 ml plasma.

*Epinephro-phlebography* The examinations were performed by manual injection, the amount of contrast medium and rate of injection (1.5 to 10 ml Urografin 76 % during 2 to 3 sec) being judged in all cases except two by TV fluoroscopy of the venous filling during a test injection. The duration of contrast medium in the adrenal veins was about 5 to 10 sec. The contrast medium was allowed to flow out through the catheter immediately after completion of the phlebography in the few cases in which the catheter occluded the drainage veins. Trial injections employing hydrostatic pressure were also made in 5 cases in order

Table 3 (cont.)

| Case | Age (years)<br>and sex | Diagnosis                        | $\mu\text{g}$ cortisol 100 ml plasma |            |
|------|------------------------|----------------------------------|--------------------------------------|------------|
|      |                        |                                  | Vena cava                            | Left gland |
| 1    | 25 ♀                   | Benign essential hypertension    | 378                                  | 2 703      |
| 2    | 28 ♂                   | Benign essential hypertension    | —                                    | 2 653      |
| 3    | 20 ♂                   | Benign essential hypertension    | 37.7                                 | 2 109.7    |
| 4    | 30 ♀                   | Benign essential hypertension    | 54                                   | 1 895      |
| 5    | 31 ♂                   | Benign essential hypertension    | 31                                   | 1 820      |
| 6    | 59 ♂                   | Hypophyseal feminizing adenoma   | 30.4                                 | 1 806      |
| 7    | 50 ♀                   | Benign essential hypertension    | —                                    | 1 654      |
| 8    | 31 ♂                   | Benign essential hypertension    | 31                                   | 1 433      |
|      |                        |                                  |                                      | 643        |
| 9    | 49 ♂                   | Benign essential hypertension    | 33                                   | 1 339      |
| 10   | 49 ♀                   | Benign essential hypertension    | 24                                   | 1 075      |
|      |                        |                                  |                                      | 1 274      |
| 11   | 32 ♀                   | Benign essential hypertension    | 47.6                                 | 1 061      |
|      |                        |                                  |                                      | 81.3       |
| 12   | 41 ♂                   | Benign essential hypertension    | 27                                   | 911        |
|      |                        |                                  |                                      | 753        |
| 13   | 47 ♀                   | Benign essential hypertension    | 100                                  | 853        |
| 14   | 49 ♀                   | Pancreatitis                     | 32                                   | 803        |
| 15   | 44 ♀                   | Benign essential hypertension    | 23                                   | 615        |
| 16   | 47 ♀                   | Benign essential hypertension    | 28                                   | 576        |
| 17   | 62 ♂                   | Benign essential hypertension    | 19                                   | 541        |
| 18   | 34 ♂                   | Benign essential hypertension    | 29.9                                 | 452.9      |
| 19   | 20 ♂                   | Benign essential hypertension    | 23                                   | 245        |
| 20   | 62 ♀                   | Aldosteronoma sin                | 79                                   | 137        |
|      |                        |                                  |                                      | 122        |
| 21   | 5 ♂                    | Malignant essential hypertension | —                                    | 94         |
| 22   | 36 ♀                   | Benign essential hypertension    | 35.2                                 | 75.1       |
| 23   | 37 ♂                   | Phaeochromocytoma                | 22                                   | 42         |
| 24   | 21 ♂                   | Benign essential hypertension    | 20                                   | 42         |
| 25   | 51 ♂                   | Benign essential hypertension    | 15.5                                 | 34.2       |
| 26   | 38 ♀                   | Possible adrenal insufficiency   | 13.9                                 | 19.1       |
|      |                        |                                  | Mean value                           | 889.5      |

to obtain exactly the same rate of injection during the test injection and phlebo-graphy. A syringe without piston, attached to the catheter by means of a drip tube with wide bore attachments, was filled with Urografin 76 % in 4 cases and with the considerably less viscous Contray 280 in one case. The syringe was then raised to a maximum of two meters above the patient, but produced insufficient filling of the adrenal veins. On the other hand a new film changer (Puck, Elema-

Schonander), employed in 2 cases, permitted the injection of contrast medium to be followed on a TV monitor during phlebography itself, and obviated the need for a test injection.

## Results

The cortisol content was assessed both before and after phlebography in 5 cases and was found to vary between 2 030.5 and 16.5  $\mu\text{g}$  before the examination, and between 914.3 and 21.3  $\mu\text{g}$  after the examination, while the values obtained for samples from the vena cava remained between 23.2 and 16.1  $\mu\text{g}$ . The cortisol content was lower after phlebography when the initial value was high, but somewhat higher when the initial value was low (Table 1).

The values rose immediately after the injection of the hypophyseal hormone in the 2 cases stimulated with Synacten after phlebography. In the first case (left gland), the cortisol content rose from 457.6 to 3 713.5  $\mu\text{g}$  within 30 min, and in the second case from 542.8 to 1 735  $\mu\text{g}$  on the left side and from 483.3 to 1 695.3  $\mu\text{g}$  on the right side. The activity in both left glands fell rapidly after the maximum and a few minutes later the values dropped below the initial levels (Table 2).

The hormonal content varied considerably in the material from the previously published series of epinephro-phlebographies in which no hormonal assessments were made before the examinations (Table 3). The highest cortisol content in the blood samples taken from the 44 glands was 4 876  $\mu\text{g}$  and the lowest 19.1  $\mu\text{g}$ , while the corresponding values for samples from the vena cava were 378 and 13.9  $\mu\text{g}$ . In one case of rupture in the intraglandular veins the cortisol content was as high as 3 592  $\mu\text{g}$ , venous glandular blood could not be sampled in a further 5 cases of similar rupture.

## Discussion

*Effect of the catheter.* All catheter materials used intravascularly involve a certain though slight risk of thrombosis formation by the agglutination of thrombocytes on the surface of the catheter. It has not been proved that different materials exhibit different tendencies in this respect, but the risk of clinically significant reactions has been found to increase with the area of surface contact between catheter and blood in human arterial blood (JACOBSSON 1969, JACOBSSON et coll 1969). The intravenous administration of Dextran 70 was of prophylactic value in arteriography by reducing the agglutination. Since this procedure influences the hormonal values of the blood, it cannot be employed in conjunction with sampling for hormone analysis. Heparin was therefore used in doses of about 5 000

I U, in spite of the fact that this agent influences the coagulatory mechanism in another way and possibly causes more bleeding in the event of venous rupture. Two cases of thrombosis occurred, one in the femoral vein and the other in the vena saphena magna. However, if Dextran 70 has the same effect in venous as in arterial blood, it could be valuable for routine epinephro-phlebography. It has not yet proved possible to demonstrate that there is any diagnostic value in the selective cortisol assessments.

*Effect of increased venous pressure* The blood pressure was not affected during catheterization except when the tip of the catheter blocked the adrenal drainage vein. On the occasions when this occurred, there was often a rise or fall in the pressure at the same time as the patient experienced characteristic pain in the back on the side in question. The injection of contrast medium or physiologic saline enhanced the change in pressure. The systolic pressure sometimes rose considerably, in one case from 260 to 300 mm Hg. The blood pressure always returned to the initial level as soon as the catheter was withdrawn.

Extravasal outflow of contrast medium occurred in 6 cases of the earlier series of phlebographies, and the phenomenon has also been described by BOOKSTEIN *et coll.* (1968). The outflow most often occurs relatively peripherally in the gland, probably beginning in the special type of veins whose walls consist of a single layer of endothelial cells alone (MIKAELSSON, 1969). The damage caused temporary discomfort and pain, which required analgesic treatment. It was possible to obtain a sample of venous blood in one of these cases, and this was found to have a high cortisol content. One rupture occurred in a left gland with aldosteronoma. The tumour was removed and a haematoma around the ruptured gland was found at operation. Since publication of this series (MIKAELSSON, 1969) two glands have ruptured at phlebography. The patients were operated upon afterwards for morbus Cushing but not because of the complication. No tumours were found at bilateral phlebography or at surgery. One of the ruptures had occurred within the top of the gland but its cortex and capsule remained intact. The right gland was not damaged, but was also extirpated. In the other case the severely damaged right gland was spared while the left intact gland was removed. Megavolt radiation therapy was carried out with 3 500 rad to the hypophysis. The symptoms of morbus Cushing diminished considerably and no more adrenalectomy was performed. A latent adrenal insufficiency was present one year afterwards but it is not known if it is permanent.

"BOOKSTEIN, has described a case of left side rup-

ture during phlebography in which the entire right gland was later extirpated for aldosteronoma. Cortical hormones must still be administered, six months after adrenalectomy. BOOKSTEIN *et coll* (1968) reported that 5 out of 9 adrenal glands had suffered damage during phlebography performed in primary aldosteronism, extensive double-side rupture had occurred in one of the cases. In spite of the fact that one of the glands with an aldosteronoma was removed, no subsequent hormonal substitution was necessary. The adrenal glands are said to be particularly sensitive in this disease. NESBIT (1967) stated that the glands were frequently atrophic and delicate in cases of primary aldosteronism and called for special care to avoid their damage during surgery. On the other hand, ZIMMERMAN *et coll* (1959) considered that the gland is not atrophic if the aldosteronoma is small. SILEN *et coll* (1966) expressed the same opinion about the contralateral gland. In the series described in the present and previous studies (MIKAEELSSON 1969), only one venous rupture occurred in the 10 cases with tumours. It was one of the six instances of aldosteronoma.

The adrenal glands are described as able to maintain sufficient activity in spite of extensive resection (RICHTARDS *et coll* 1960, ROGERS 1961, SILEN *et coll* 1966, ZIMMERMAN *et coll* 1959). Only temporary substitution therapy was required in practically all cases after subtotal resection (up to 90 per cent) of adrenal tissue in cases subjected to surgery for hypertension. SKELTON (1955) in a study on rats stated that there was regeneration of the adrenal cortex 'to a marked extent' after resection to the degree that only subcapsular remnants were left *in situ*. Although an adrenal gland will not necessarily suffer total destruction even after venous rupture with extensive outflow of contrast medium, such a danger exists. It is also possible that a gland could have been destroyed before phlebography, e.g. by thrombosis of its veins. If there has been rupture of the gland on one side, it is doubtful whether the other gland should be examined. The minor outflow of contrast medium occurring during test injection in a case of the present series and in a case described by BOOKSTEIN *et coll* (1968) increased considerably during the actual phlebography in both instances. The slightest leakage of contrast medium is thus an indication for the termination of the examination.

An improved injection technique would probably be of value in avoiding the intraglandular complications. The only means of assessing a suitable flow of contrast medium has usually been by giving test injection under fluoroscopic control and noting any pain experienced. The subsequent manual injection during actual phlebography has constituted only a rough simulation of the test, however. Even if it were possible to maintain a constant rate of flow by hydrostatic pressure or some form of mechanical injection device, the disadvantage that two injections are needed for each phlebography would still exist. Although recording of the test injection on a disc or video tape could be useful if a rupture

were to occur (recordings of this kind were actually made in 5 cases although it was never necessary to use them), probably the best safeguard is a film changer that allows the injection to be followed on a TV screen throughout the examination proper. This has been possible with the new film changer Puck, which was tried out during two of the last examinations. The filling of the adrenal veins with contrast medium could be followed in detail and controlled by gradually increasing the rate of injection until a suitable degree of filling of the veins had been achieved. If a leakage of contrast medium should nevertheless begin to occur, the injection can be discontinued at once while the leakage is still small.

*Effect of the contrast medium* Although the toxicity of modern contrast media has been considerably reduced, it is nevertheless recognized that they can have disadvantageous effects in concentrated form, chiefly because of their high osmotic pressure, especially if the positive ion is Na (LINDGREN & TORNELL 1958, LINDGREN et al. 1968, TORNELL 1969). A high concentration of the contrast medium has been necessary in the epinephro-phlebographies in order to obtain the required diagnostic information. The contrast medium employed (Urografin 76 %) is a diatrizoate, 90 per cent of which is a methylglucamine salt. It has frequently been administered in relatively large total amounts (100 to 150 ml) during the examinations, which on the right side in particular have often called for repeated small test injections before the adrenal vein could be located. No effect on the system as a whole has however been observed. The dose administered during the actual phlebographies ranged from 1.5 to 10 ml, depending on the capacity of the veins in and around the gland as well as on the extent of reflux of the medium back into the large veins. It has not been possible to estimate the exact dose of contrast medium to the glands themselves. In the few cases of total occlusion of the adrenal drainage vein by the catheter and where there were few communicating vessels, the intraglandular veins and, in part the capillaries as well, became well filled with about 1.5 ml contrast medium, which probably constitutes the capacity of the venous system of the gland. Thus, only a small quantity of contrast medium normally came in contact with the vessels of the gland and for a relatively brief period, i.e. about 5 to 10 sec.

Eight glands, previously examined by phlebography, were inspected and palpated during surgery, and a further 18 glands were also examined histologically after extirpation in the previous study (Mikaelsson 1969). No effect from the contrast medium or the increased venous pressure during phlebography was observed.

*Hormone analyses* The position of the catheter in the adrenal vein must be identical when taking both samples in order to obtain perfectly comparable blood samples before and after phlebography. This can best be checked on the left

side, where it is always possible to position the catheter without occluding the vein if the tip is located below the point of inflow of the inferior phrenic vein. A post-mortem study (MIKAELSSON 1970) has also indicated that this part of the vein is considerably wider than the catheter, which in this position therefore causes no major obstruction to the flow of blood. It can thus be assumed that the hormonal content of the sampled blood corresponds to the physiologic conditions at the time of the examination. On the right side it is more difficult to assess the exact position of the catheter tip. However, any blockage or varying mixture of extraneous blood during sampling must be infrequent (Table 3).

The production of cortisol in the 5 cases studied both before and after phlebography (Table 1) fails to indicate that the values were affected to any great extent by the injections of contrast medium. Although these values fell in 3 cases in which the initial values were high, they rose in at least one case in which this value was low. The low cortisol contents before phlebography in the small series (Table 1) disclose that the post-phlebography values in the large series (Table 3) need not have been influenced by the contrast examinations. This impression is strengthened by the fact that all 3 glands stimulated with Synacten after phlebography could achieve high cortisol production.

WEINHEIMER *et coll.* (1963) and BETTE *et coll.* (1964), performing adrenal catheterizations, reported similar but not quite such varying results as in the present study. The values in the first-mentioned studies ranged from 39 to 208  $\mu\text{g}$  cortisol in a series of 10 cases with congenital cardiac defects. The catheter positions were not checked by phlebography, however. HUME & NELSON (1954), who led off blood for serial analyses from the left adrenal gland of dogs through a surgically inserted catheter noted mainly low but varying values during the post-operative period, they considered that this was because ACTH is secreted intermittently from the hypophysis during rest.

The results of these investigations indicate that the activity of the adrenal glands varies within wide limits in a material of blood samples definitely obtained from them. A number of values do not even exceed the values in samples taken from the vena cava. No patients, except one, exhibited clinical signs of adrenal insufficiency. It therefore seems probable that there is a certain intermittence in the cortisol secretion of the glands, which makes any diagnostic conclusions from the individual hormonal values obtained difficult.

### Conclusions

No damage to the adrenal glands by epinephro phlebography, except for a few venous ruptures, occurred in the material.

The cortisol production of the glands in patients at rest varies to a degree that

individual cortisol values in blood from the glands fail to provide any reliable information about their activity

### Acknowledgements

The author takes this opportunity of thanking Prof R. Luft and Ass Prof H. Low of the Endocrinologic Clinic Karolinska sjukhuset, Stockholm for their support and help without which this work would have hardly been possible. The aid granted by The Swedish Medical Research Council (Project B69 61P 2601 01) is also gratefully acknowledged.

### SUMMARY

Intraglandular venous ruptures in a material of adrenal glands subjected to phlebography and an improved injection technique are described. The glands possessed hormonal activity after the procedure and the cortisol values had not fallen to any greater extent; the activity became greatly increased on stimulation with an ACTH preparation.

### ZUSAMMENFASSUNG

Intraglanduläre Rupturen der Venen während Phlebographie der Nebennieren und eine verbesserte Injektionstechnik werden beschrieben. Nach Phlebographie zeigten die Nebennieren eine Hormonausscheidung und die Cortisol Werte waren unbedeutsam gefallen. Die Aktivität stieg nach Anreizung mit einem ACTH Präparat stark an.

### RÉSUMÉ

L'auteur décrit des ruptures veineuses intra-glandulaires au cours de phlebographie des surrenales et présente une technique d'injection améliorée. Les glandes avaient conservé leur activité hormonale après cet examen et la dose de cortisol n'avait pas du tout baissé. L'activité des surrenales a été très augmentée par la stimulation faite au moyen d'une préparation ACTH.

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## ARTERIOGRAPHY IN ARTERIAL GUNSHOT WOUNDS

By

JIRI GIRL

Gunshot wounds of the extremities occur but rarely in the angiologic practice of the radiologist. They may be incurred *interalia* either as a result of an attempt at suicide or by accident. In addition to the destruction of the soft tissues, the lesion may involve the vascular, osseous or nervous systems and often also other systems. A gunshot injury of an artery of the extremity may on the one hand manifest itself by local signs, among which bleeding is the most serious or, on the other hand, by signs produced by a lesion to the peripheral blood supply, the most feared of which is gangrene of the extremity. The local and peripheral signs are however sometimes atypical, and therefore an exact diagnosis may be possible only by arteriography.

The reports in the literature concerning arteriography following gunshot wounds of the extremities are few and far between. They all indicate the unreliability of the clinical signs which do not always reflect the true condition, thus lending support to the need for arteriography (BERK 1963, BRADHAM et coll 1964, KALLONEN 1966, LUMPKIN et coll 1958, O'NEILL & KILLEN 1961, VOGT 1963).

Arteriography is regarded indicated in cases of (1) unarrested bleeding, (2) probable arterial occlusion due to arterial thrombosis or arterial stenosis caused by a compression haematoma (ischemia of the extremity), (3) possible



Fig 1



Fig 2

Fig 1 Case 1 Injury of the left leg by a cartridge splinter. Arteriography 33 days after the injury. Displacement and stenosis of the peroneal artery in the region of the foreign body, the anterior tibial artery was not contrast filled. (An aneurysm of the artery was found at operation)

Fig 2 Case 2 Two gunshot wounds in the left axillary region persistent haemorrhage. Arteriography 37 days after the injury. Occlusion of the axillary artery due to a false aneurysm and resulting thrombosis abundant collateral circulation.

arterial aneurysm or arteriovenous shunt (flaps and whirls), (4) atypical symptoms which may be of vascular or nervous origin and (5) postoperative control or vascular reconstruction.

Some authors do not consider this examination necessary when the clinical evidence is sufficient (MORTON *et al.* 1966).

We have had the opportunity during the last nine years to examine 14 cases of gunshot wounds of the extremities. These are analysed in the present communication and four illustrative case reports are included.

All the fourteen patients were males ranging in age from 19 to 24 years. The cause of the injury was suicidal attempt in nine and accident in five patients, and the locations were respectively in the upper extremity in nine and lower extremity in five. Arteriography was in three patients performed on the day of injury and in seven there was an interval of 10 to 69 days between injury and arteriography. Postoperative control in four of the patients caused re-operation to be performed in one of them.



Fig 3 Gunshot wound of the left axillary region with a comminuted fracture of the humerus. Arteriography on the day of the injury showed a defect in the wall of the axillary artery and a false aneurysm.



Fig 4 Case 3 Gunshot wound of left axillary region. Arteriography 15 days after injury. Aneurysm of axillary artery about 15 mm diameter, comminuted fracture of scapula.

*Preparation of the patients and method of examination* Following the trauma sustained, all the patients were psychially disturbed and frightened before the examination. For this reason they were informed about the technique of percutaneous arteriography and the consequent possibility of saving the extremity. Some of the patients were given sedatives. Arteriography of the upper extremity was always performed via the right femoral artery, the tip of the catheter being placed, when possible, peripheral to the origin of the vertebral artery. Arteriography of the lower extremities was carried out by catheterization of the femoral artery on the injured side, and the catheter was inserted into the common iliac artery.

For the examination of the upper extremities 10 ml Mesocain Spofa 1% and for the lower extremities 20 ml of this medium were injected intra arterially. Any pain caused by the contrast medium injected for the fluoroscopic control was relieved by 1 to 2 ml of Dolsin Spofa subcutaneously. An amount of 20 to 25 ml of Urografin 50% or Verografine were injected as contrast medium by means of a Gidlund syringe at a pressure of 3 kg. The films of the upper extremities were obtained at intervals of 0.5 to 1 second and of the lower extremities at intervals of 1 to 2 seconds with Elema-Schonander and Philips film changers.



Fig 5 Gunshot wound of the left subclavicular region. Arteriography on the day of injury. Arteriovenous shunt in the vicinity of the gunshot channel in the lung ( $\rightarrow$ ), dilatation of the vein and poor filling of the artery containing the catheter ( $\rightarrow$ )



Fig 6 Gunshot wound of the left axillary region, condition after reconstruction of the artery with a vein graft. Arteriography eight and a half months after the injury. Occlusion of the axillary artery and poor collateral circulation

The arteriographic findings in the fourteen patients were as follows

Lesion of the small arterial branches due to haematoma near the gunshot channel, the main artery being intact

Interrupted artery

Arterial aneurysm

Arteriovenous shunt

Normal finding (gunshot wounds of both thighs)

In four of the patients, postoperative arteriography resulted in the following findings

Occlusion due to thrombosis

Ligation of artery

Arterial aneurysm

2  
2  
2  
3  
1  
2  
1  
1

### Illustrative case reports

**Case 1** Male, 20 years old, wounded accidentally by a cartridge splinter. Arteriography 33 days after the injury resulted in no filling of the anterior tibial artery, the peroneal artery was displaced and stenosed at the level of the splinter. Operation revealed aneurysm of the anterior tibial artery (Fig 1)

**Case 2** Male, 20 years old, after suicide attempt had two gunshot wounds in the left axillary region with disturbance of the blood supply to the extremity and persistent haemorrhage. Arteriography 37 days after the injury disclosed interruption of the axillary artery and abundant collateral circulation, the branches of which were stretched and of irregular calibre due to a haematoma (Fig 2)

Fig 7 Case 4 Gunshot wound of the right femur. Arteriography was performed after the first operation at which the femoral artery was sutured and the femoral vein ligated. Aneurysm of the femoral artery at the level of the gunshot channel (arrows). (No aneurysm was found at the second operation.)



Fig 7

Fig 8 Gunshot wound of the left femur. Operative revision suggested an intact femoral artery. Arteriography two months later because of persistent circulatory disturbances revealed occlusion of the femoral artery at the level of the pseudarthrosis of the femur and stenosis at its distal end.



Fig 8

Case 3 Male 20 years old with accidental gunshot wound to the left axilla with injury of the brachial plexus, fracture of the scapula and pain and congestion of the arm. Arteriography 15 days after the injury revealed an aneurysm, 6 mm in size of the axillary artery with slight arterial stenosis (Fig 4). No operation was performed.

Case 4 Male, 23 years old with accidental gunshot wound of the distal end of the right femur with considerable bleeding. Suture of the injured artery and ligation of the femoral vein were carried out at the first operation. The haemorrhage persisted and the pulse was not palpable at the arteria dorsalis pedis but present at the posterior tibial artery. Arteriography 37 days after the first operation disclosed a 13 mm  $\times$  15 mm large sacular aneurysm. Displacement and stenosis of the femoral artery were present due to the haematoma at the level of the gunshot channel. At the second operation the femoral artery was intact but 1.5 cm above the suture a small branch was bleeding. Ligation was performed and the haematoma was evacuated; the aneurysm could not be located (Fig 7).

### Discussion

The patients with gunshot wounds were much affected both psychically and physically. There was nevertheless no need for special preparation and the examinations were carried out without complications. Arteriography was performed by catheterization with satisfactory results, and any haemorrhage that occurred was not increased.

As was evident on comparing the arteriographic and operative findings (Case 4), a lesion to a small arterial branch was serious enough to cause

abundant and prolonged bleeding although the main artery of the extremity remained intact. In other instances (cf. Case 3), on the other hand, the main artery of the extremity was damaged but the haemorrhage subsided spontaneously after a few days. Arterial occlusion explained convincingly the peripheral ischemia but the arteriographic appearances failed to indicate whether the artery was completely interrupted or affected by thrombosis produced by a false aneurysm (Case 2).

Arterial aneurysms produced by injury to the arterial wall ranged in size from 5 to 15 mm, their exact localization by arteriography permitting their localization and resection even in grossly damaged tissue. It was only in Case 1 that the aneurysm was not outlined and found only at operation.

With arteriovenous shunts in the subclavicular region it was important to assess their exact location since entry to this region depended on the position of the shunt. The approach was either extrathoracic with osteotomy and osteosynthesis of the clavicle, or by thoracotomy.

Postoperative arteriographic appearances indicated the changes developing in the blood supply and led in Case 4 to re-operation. An aneurysm which had not been found at the first operation was then located. This is the reverse of what occurred in Case 1.

Experiences have indicated that arteriography has fulfilled all expectations and that it should be undertaken in association with surgery, as early as possible, before healing in the damaged tissue induces irreparable fibrous changes that will preclude subsequent vascular reconstruction.

## SUMMARY

The indications and technique for the arteriographic examination of gunshot wounds of the extremities are described. The results obtained are illustrated by four typical cases of the total 14 cases of the material.

## ZUSAMMENFASSUNG

Die Technik und die Indikationen für die angiographische Untersuchung von Schussverletzungen der Extremitäten werden beschrieben. Die Untersuchungsergebnisse von vier typischen Fällen von einem Gesamtmaterial von 14 Fällen werden angegeben.

## RÉSUMÉ

Description des indications et de la technique de l'examen arteriographique des plaies des membres par balles. L'auteur presente les resultats obtenus au moyen de quatre cas typiques sur son total de 14 cas.



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## EXCRETION OF SODIUM METRIZOATE THROUGH THE LIVER DURING UROGRAPHY

by

OLLE OLSSON

The nature of an intravenous cholegraphic or urographic agent is based on the structure of the contrast medium molecule. The 5 position in the aromatic ring seems to be the decisive factor as to the lipophilic or hydrophilic nature of the medium, the former constituting a cholegraphic, the latter a urographic agent. This may also be expressed as the protein binding capacity of a contrast medium.

As pointed out by LASSER *et coll* (1962), the more strongly protein bound contrast media appear to be excreted preferentially in the bile. In the trisobenzoate acid compounds, the absence of a prosthetic group at the 5 position in the benzene ring seems to determine the strong binding to albumin. This is the case with Urokon and specifically with Cholegrafin. The latter is therefore a cholegraphic medium, and on the same but slightly weaker grounds Urokon (sodium acetrizoate) also often leads to gallbladder filling at urography. WOLLEY *et coll* (1957) after intravenous administration of Urokon sodium 70% for urography in 'standard doses' could demonstrate gallbladder filling in twelve out of twenty five patients 2 hours after its injection. Media such as Hypaque and Urografin (sodium diatrizoate) on the other hand exhibit weak protein binding.

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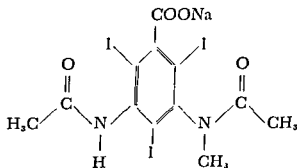
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Fig 1 Bilateral hydronephrosis and hydroureter. Selective angiography of both kidneys using 12 ml Isopaque as contrast medium. Filling of the gallbladder occurred 50 minutes after the first injection.

and seldom fill the gallbladder. SEGALL (1969) in reporting on contrast filling of the gallbladder at urography in five subjects pointed out the rarity of this phenomenon.

Sodium metrizoate is a contrast medium marketed under the name Isopaque (Nyegaard & Co, Oslo) and consists of a balanced mixture of sodium, calcium, magnesium and N-methylglucamine salts of metrizoate acid. It is closely related to sodium diatrizoate as may be seen from the chemical formulas



Metrizoate sodium (Isopaque) (sodium N-methyl-3,5-diacetamido-2,4,6-triiodo benzoate)

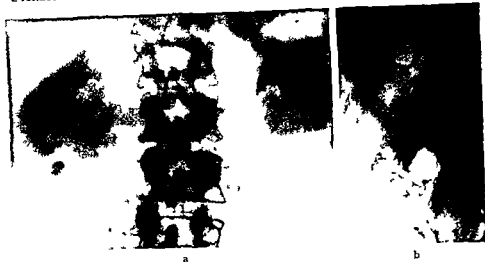
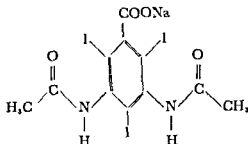


Fig 2 Right side renal colic due to ureteric stone (no pain on examination) a) Stasis on right side 3 minutes after injection b) Filling down to the stone in the ureter 20 minutes later and also filling of the gallbladder



Diatrizoate sodium (sodium 3,5-diacetamido-2,4,6-triiodobenzoate)

We have found that filling of the gallbladder is fairly often obtained in connection with the injection of the contrast medium for urography or angiography. Filling of the gallbladder may be seen already during the actual examination (Fig 1) but it seldom occurs under ordinary conditions. In a few patients, it had been subjected to contrast medium examinations.

tions in the urinary system

on examination of the urinary system on the same day. The interval between the injection and the time of filling was about 4 hours. In a series of 25 patients, whom ordinary conditions had been demonstrated at urography, no filling of gallbladder could be observed in any one of the patients on examinations



Fig 3 Right side renal colic a) Marked stasis b) Filling of the gallbladder in connection with the actual examination

formed 5 hours and 24 hours respectively after urography, specifically to see if such filling occurred. Filling of the gallbladder in connection with normal urography using Isopaque as contrast medium is thus a rare phenomenon.

On the other hand, the gallbladder is often contrast-filled at urography or angiography if stasis in the urinary pathways is present. This occurs more often with sodium metrizoate than with the diatrizoate media. We have encountered several cases in which during urography in connection with an attack of pain (sometimes persisting throughout the examination) a marked or only slight stasis was present on one side and at the same time filling of the gallbladder was observable (Figs 2 and 3) during the actual examination. When this happens it may be used as an extra sign of diagnostic importance when the acute examination is performed for the purpose of a clinical differential diagnosis between an attack of cholelithiasis and urolithiasis, and if signs of stasis at urography are slight or absent when the examination is performed after the subsidence of pain.

Filling of the gallbladder during the actual examination can be slight but may sometimes be quite marked. If minimal, an increase in concentration will usually occur during the following hours and good filling may persist and be seen on the next day.

We also have noticed filling of the gallbladder in a patient who immediately after injection of the contrast medium had a marked fall in blood pressure. No excretion could be seen through the kidneys until the blood pressure had risen.

Filling of the gallbladder occurred in a patient with polycystic renal disease,



Fig 4 Uremia and respectively heterotopic excretion of the contrast medium a) In connection with selective nephroangiography the gallbladder which contained a large stone was filled b) Infusion urography (250 ml Iopaque) Excretion of the contrast medium through the liver (filling of the gallbladder and the colon on right side)

this represents a borderline case of heterotopic excretion of contrast medium, as in uremia. This type of excretion thus seems to be the same with sodium metrizoate as with other contrast media (Fig 4)

The difference in excretion in the bile between the salts of metrizoate and diatrizoate acids is not related to a great difference in the chemical composition, the only difference in this respect being the addition of a methyl group in the 3 position in the metrizoate compound. This may affect excretion under certain conditions. Another factor seems more plausible, however, in relation to the excretion of the contrast medium through the liver in patients with acutely impaired renal excretion in renal colic. Dawson *et coll* (1968) in experiments with  $^{125}$ I

was found to be a two-rate process, with half-lives of about 15 minutes and 2 hours. As compared with the corresponding figures for sodium diatrizoate in the first of the two rate processes, related to available water space, sodium metrizoate was found to have a considerably shorter half-life, i.e. 15 minutes as compared with 52 minutes (Stokes & Ter



PERGOSSIAN 1964) It is probably this difference that explains the excretion of the sodium metrizoate through the liver, with filling of the gallbladder more rapidly if acute, unbalanced stasis is present in the urinary pathways. The choice by the organism of the liver route of eliminating a contrast medium, which under ordinary conditions offers specifically rapid excretion through the kidneys, may be looked upon as a conditional safety resort.

## SUMMARY

Filling of the gallbladder occurs at urography more often with sodium metrizoate than with sodium diatrizoate especially in acute urinary stasis in connection with unilateral renal colic in longstanding stasis and in some other conditions. The molecular structure of the contrast medium as related to excretion and the influence of specific half life values of the excretion upon conditional selection of the excretion organ are discussed.

## ZUSAMMENFASSUNG

Füllung der Gallenblase während Urographie wird häufiger nach Injektion von Natrium Metrizoat als nach Injektion von Natrium Diatrizoat erhalten besonders wenn akute Abflussbehinderung mit unilateraler Nierenkolik vorhanden ist und weiter bei chronischen Abflussstörungen und anderen Erkrankungen. Die Molekularstruktur des Kontrastmittels hinsichtlich der Ausscheidung und der Einfluss der spezifischen Halbwertszeiten auf die selektive Wahl der Ausscheidungswege werden diskutiert.

## RÉSUMÉ

L'opacification de la vésicule biliaire au cours de l'urographie est plus fréquente avec le metrizoate de sodium qu'avec le diatrizoate de sodium, en particulier dans la stase urinaire aiguë due à une colique néphrétique unilatérale, dans la stase de longue durée et dans certaines autres affections. L'auteur examine l'effet de la structure moléculaire du moyen de contraste sur l'excretion et l'influence de la demi-vie spécifique de l'excretion sur le choix de l'organe excréteur.

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## RELATIONS BETWEEN THE CERVICAL SPINE AND THE VERTEBRAL ARTERIES

by

PAUL CONSTANTIN and COTUNA LUCRETIA

Changes in the extracranial parts of the vertebral arteries play an important part in circulatory disturbances in the basivertebral region. Post mortem examinations by HUTCHINSON & YATES (1956), VIRTAMA & HIVALO (1957) and HADLEY (1958) have demonstrated that cervical arthroses, particularly those of the uncovertebral joints are liable to produce displacement or compression of the vertebral arteries.

*Material and Methods* Vertebral arteriography with  $\text{BaSO}_4$  paste was performed in some 200 autopsies and films obtained in six projections with flexion, extension and rotation of the head. The cervical spine was then removed and examined microscopically. The observations were compared with the clinical symptoms and signs of the subjects during life.

*The anteromedial part of the vertebral arteries is in contact with the anterior third of the lateral parts of the uncovertebral joints from C2 to C6. The remainder of the arterial circumference articulates with the osseous perimeter of the foramen transversarium. The development of osteophytes at the margins of the uncovertebral joints depends to some extent on the condition of the*



Fig 1



Fig 2

Fig 1 Osteophytes displace but do not compress the vertebral arteries

Fig 2 Osteophytes at the lower right margin of C5 compress the vertebral artery and hold it tightly. Atheromatous stenosis of the left vertebral artery (arrow)

arterial wall. As long as this is not atheromatous osteophytic formation in a lateral direction will be prevented by the blood pressure and the pulse wave, the osteophytes may, however, develop in a more cranial direction. Lateral osteophytes may occur when the arterial wall is atheromatous, they displace but do not compress the artery and the eventual stenosis at this level is due to atheroma (Fig 1).

Laterally directed osteophytes located medially at the lower margin of the foramen may, however, compress the vertebral artery, which at this level is held rigidly by the foramen (Fig 2).

The vertebral arteries do not normally come in contact with the intervertebral joints. The surfaces of these slant inwards and backwards. Thus the anterior half of the internal margin of the joint apophysis never actually touches the vertebral artery even during the most extensive movements of the spine. The vertebral arteries may on the other hand be affected by intermittent contact with the intervertebral apophyses during movement of the spine if (1) the transverse diameter of the intervertebral joint be increased, or (2) the movement be abnormal.



Fig 3 Osteophytes on the inferior articular surface of the vertebra extend over the foramen and reduce its diameter

Arthrosis is the most frequent cause of enlargement of the transverse diameter of the articular surfaces of the intervertebral joints particularly through anteromedial osteophytes. In the course of abnormal movements the anteromedial margin of the upper articular area rubs against the artery. The intermittent contact between the artery and adjacent bone does not prevent the development of osteophytes. Transient contacts between the artery and bone margins may possibly result in injury to the vasa vasorum with subsequent degeneration and scar formation of the arterial wall. This area is more or less rigid and the artery may be angled at this level during movements of the spine so that its lumen temporarily becomes almost completely reduced.

The medial wall of the canal for the vertebral arteries is formed by the respective uncovertebral joints. In the standard oblique view of the cervical spine the deformation both of the intervertebral joints and the osteophytes of the uncovertebral joints are visible but their relationships to the vertebral artery cannot be exactly estimated, this is however possible in the a p projection.

Osteophytes on the upper articular surface play an essential pathogenic part in their relations with the vertebral artery and will be seen to protrude into the canal of the vertebral artery in the a p projection. Osteophytic changes on the anteromedial aspects of the lower articular surface of a vertebra are however, difficult to identify in this view, and are better demonstrated in oblique views in flexion, when the inferior surface of the upper vertebra slides forward.

Osteophytes on the anteromedial margin of the inferior articular surface extend over the posterolateral segment of the foramen, sometimes halving its true diameter (Fig 3). These osteophytes may compress the vertebral artery in flexion. The compression of the lumen of the artery is proportional to the size of the osteophytes, the compression may sometimes also be evident in the



Fig 1



Fig 2

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Fig 5



Fig 6

Fig 5 Osteophytes on the anterior half of the upper joint surface reduce the diameter of the foramen

Fig 6 Experimental set up. Forced rotation combined with extension may compress the vertebral artery between two osseous planes

is supposed to release violent reflex muscular contraction and the neck remains fixed in this position. This mechanism, which the authors reproduced experimentally (Fig 6), represents a more logical reason for the fixation of the neck and may occur following sudden movement of the cervical spine, clinically represented by hemicrania and signs of irritation of the sympathetic nerves.

The following films are necessary to demonstrate the unilateral subluxation during the movement: a p, lateral and oblique in flexion and in extension. These allow a detailed analysis of all the normal and pathologic aspects of the cervical spine and an assessment of the relations between it and the vertebral arteries.

It is recognized that the degree of atheromatous degeneration of the vertebral arteries, although minor, is still generally more advanced than that of other major arteries. Gross atheromatosis of the vertebral arteries, although creating chronic insufficiency in the basivertebral circulation, is well tolerated as long as the vertebral arteries are not compressed by adjacent bony structures.

Compression of the arteries during movements of the spine may suddenly interfere with the blood, release the clinic syndrome, and, by damaging the arteries, increase the degeneration of the vessel. The syndrome of basivertebral ischemia from disturbance of the circulation in the extracranial segment of the arteries is thus primarily dominated by the relations between the spine and the vertebral arteries. Their radiologic analysis is obviously of great clinical significance in the appreciation of the syndrome.



Fig 4 Lateral views Osteophytes on the inferior articular surface of C5 compress the vertebral artery in flexion (a) but the compression disappears in extension (b)

lateral view (Fig 4 a) On extension of the spine, the vertebrae are tilted posteriorly and the compression of the artery disappears. As long as the movement takes place within physiologic limits, no compression of the vertebral artery is produced by deformed upper articular surfaces. Compression of the vertebral arteries may, however, occur in hyperlordosis with small or moderate posterior interarticular displacement and when the anterior half of the upper joint surface is enlarged (Fig 5). The posterolateral part of the artery will be compressed in proportion to the degree of hyperlordosis and the size of the osteophytes.

Unilateral subluxation is an abnormal movement of the cervical spine produced during rotation by asymmetry of the two articular surfaces to the intervertebral joint. This asymmetry occurs either as a sequela of injury or deformity of the joint. If the deformation of the articular surface be marked and co-existent with osteophytes at the margins of the unvertebral joints at the same level, forced rotation combined with extension of the spine may compress the vertebral artery in the narrow space between the two affected points. Such an injury

## SKELETAL AND TOOTH DEVELOPMENT

A methodologic investigation

by

B LILIEQUIST and M LUNDBERG

Methods for the determination of a child's growth and development are of great value from both the medical and odontologic points of view. Four systems have been used, viz. determinations of the skeletal age, dental age and morphologic age, as well as the sexual maturity. The usefulness of the last mentioned method is limited by the fact that it can be applied only after the inception of puberty.

The method commonly applied for the assessment of the physiologic age of the subject has been the determination of the skeletal age. The skeletal system develops, grows and matures along definite lines from a primary ossification centre to fully developed bone. This process can be investigated radiologically. The skeleton matures along several lines, and the process comprises differentiation, growth and change of shape. The changes start during fetal life through the ossification of the diaphyses of the longer and shorter tubular bones. Ossification of the epiphyses of these bones and of the centres for the small bones in the wrist and ankle begins during the last part of the pregnancy, and the talus and

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## SUMMARY

Vertebral angiography with barium sulphate paste was performed post mortem in 200 cases. The films obtained were reviewed together with the clinical history, roentgenologic signs and pathologic findings. The significance of changes in the cervical joints upon the vertebral arteries is described and discussed.

## ZUSAMMENFASSUNG

An 200 Leichen wurde eine post mortem Angiographie mit Bariumpaste vorgenommen. Die erhaltenen Filme wurden roentgenologisch analysiert und mit den klinischen und pathologischen Befunden verglichen. Die Bedeutung der Gelenkveränderungen und deren Einfluss auf die Vertebralarterien wird besprochen.

## RÉSUMÉ

Les auteurs ont fait des angiographies vertébrales post mortem avec une bouillie de sulfate de baryum dans 200 cas. Ils ont comparé les films ainsi obtenus à l'histoire clinique aux signes radiologiques et aux résultats de l'examen anatomo pathologique. Les auteurs décrivent et analysent l'effet des lésions des articulations cervicales sur les artères vertébrales.

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and substituting others with a more protracted course of change. Other methods, based on the fact that different ossification centres appear in a definite time sequence, have also been elaborated. These methods are complicated and entail the taking of a considerable number of roentgenograms of large parts of the body (ELGENMARK 1946). By counting the number of ossification centres present a rough estimate of the skeletal maturity may be made. These methods, however, are only applicable during the period in which new ossification centres appear, i.e. during the first years of life.

Many of the methods briefly reviewed are complicated, some are based on subjective valuations and others on extensive material. Even if the increase in the size and the change in the form of the skeleton are two different aspects of the skeletal maturity, it is obvious that they are interconnected. They take place during the same period of time, and when growth stops the skeleton is also completely developed, i.e. is mature and has its final form.

Most of the standards (TODD 1937, GREULICH & PYLE 1959, SCHMID & MOLL 1960) are either dated or are based on examinations of subjects under growing conditions and surroundings other than are common in Sweden, and it is questionable whether they are applicable to a Swedish material. TANNER (1961) considered that American children are more developed than for example Dutch or English children at the same chronologic age. If two American standards viz. of TODD (1937) and GREULICH & PYLE (1959) are compared, it is evident that the children in the later investigation are somewhat more developed than those in the earlier one. EKLOF & RINGERTZ (1967) have elaborated a simplified method for the determination of the skeletal age of a Swedish material based on SCHMID & MOLL's method, but do not offer any opinion as to whether there is a difference as compared with other materials.

Tooth development and the age of the teeth have generally been judged by recording the number of erupted teeth. Thus, however, is a crude method, as only the number of teeth and not the time when they erupted can be judged. A much better method is with the help of roentgenograms to indicate the different developmental stages of a tooth from its first calcifications to its full development, which gives the actual situation at the time of the examination. Several standards have been devised for this purpose (LOGAN & KRONFELD, 1933, KRONFELD 1935 and SCHOUR & MASSLER 1941, *inter alios*). LOGAN & KRONFELD's and SCHOUR & MASSLER's norms for tooth development have been exposed to severe criticism by BRALER & BAHADOR (1942) and GARN *et coll.* (1959) *inter alios* who have pointed out that the ranges in the earlier investigations are all too narrow. GARN *et coll.*, who studied three stages in the development of the molars and premolars of the lower jaw, described ranges that were three times as wide as those of the earlier investigators. It would be valuable if it

carpal, and sometimes the cuboid as well are ossified at birth. The process of ossification goes on during all the growing years and is completed with the ossification of the growth plates. This implies the completion of the skeletal growth as well as the maturing process.

The process of differentiation may be investigated by determining the number of ossification centres during different periods. The growth process may likewise be gauged by quantitative measurements. The process of maturing, which consists in a change in the form of the bones, cannot, on the other hand, be directly measured. A number of means have been elaborated for the determination of the skeletal age based upon these three different aspects. Measurements of the length or surface area of individual bones constituted the dominant approach in the earlier methods. More recently, attempts have been made to determine the skeletal age by investigating the changes in the form of different bones, the investigations being based on so called maturity indicators. The quantitative methods depend on the assumption that even if the growth and the changes in the form of a bone constitute two different aspects of the process of skeletal maturing, these are nonetheless strongly correlated to each other, and that the change in the form is part and parcel of the longitudinal growth. From these points of departure SCHMID & MOLL (1960) produced an atlas for the determination of the skeletal age. The method has many advantages, as it is simple, requires only one film of the left hand in which 11 ossification centres and epiphyses in all may be examined and the result given in figures. Earlier methods based on longitudinal or surface methods have been severely criticized, partly on the grounds that with these the results are correlated more to the longitudinal growth of the child than to the age. TODD (1957) and later GREULICH & PYLE (1959) therefore produced an atlas with the help of which the skeletal age is determined through comparisons between different reproduced standards representative of every age group. Even if this method is theoretically more correct, its applicability in practice is entirely dependent on subjective assessments. MAINLAND (1957) criticized these methods from the points of view adduced above, and attempted to incorporate the process of maturing in the measuring results by performing the measurements in such a way that the changes in the form of the bone could also be calculated.

ACHESON (1957) and TANNER et coll (1962) elaborated by means of maturity indicators a system of scoring in which every ossification centre was allotted points according to the degree of maturity. GARN et coll (1967) reported that different ossification centres must have different weights assigned, as changes in certain bones are slight or absent for a long period while other centres change. EKLÖF & RINGFELTZ (1967) have to a certain extent modified SCHMID & MOLL's method by excluding certain bones that are not changed to any degree worth mentioning,

and substituting others with a more protracted course of change. Other methods, based on the fact that different ossification centres appear in a definite time sequence, have also been elaborated. These methods are complicated and entail the taking of a considerable number of roentgenograms of large parts of the body (ELGENMARK 1946). By counting the number of ossification centres present a rough estimate of the skeletal maturity may be made. These methods, however, are only applicable during the period in which new ossification centres appear, i.e. during the first years of life.

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**Table 1**  
*Distribution of material according to age and sex*

| Number of children | Age group |      |      |      |       |       |       |       | Total |
|--------------------|-----------|------|------|------|-------|-------|-------|-------|-------|
|                    | 6.5—      | 7.5— | 8.5— | 9.5— | 10.5— | 11.5— | 12.5— | 13.5— |       |
|                    | 7.5       | 8.5  | 9.5  | 10.5 | 11.5  | 12.5  | 13.5  | 14.5  |       |
| Girls              | 18        | 25   | 20   | 15   | 22    | 18    | 15    | 15    | 148   |
| Boys               | 25        | 22   | 14   | 19   | 19    | 15    | 15    | 11    | 139   |
| Total              |           |      |      |      |       |       |       |       | 287   |

were also possible for the assessment of tooth development to use numeric values suitable for statistical processing.

Only a few studies have been made in which the three methods for the determination of the physiologic age, viz. determination of the skeletal age, the tooth age and the morphologic age have been correlated. This especially applies to the connection between skeletal age and tooth age. CATTELL (1928) investigated the correlation between tooth age expressed as the total number of erupted teeth and the result of determination of the skeletal age from measurements of bones in the wrist and ankle. DEMISCH & WHARTMAN (1956) reported partial correlation between the skeletal age determined with the method of GREULICH & PYLE and the degree of calcification of a third molar of the lower jaw.

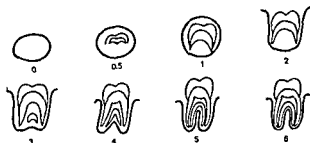
The aim of the present work was first to investigate the reliability of the method used by SCHMID & MOLI, secondly to devise a means of determining the tooth age with indication of numeric values, and thirdly to correlate these two methods. An investigation was carried out to ascertain whether there was any difference between boys and girls in skeletal age determined by the SCHMID & MOLI method and to tooth age according to the new method. An attempt at a simplification by reducing the number of measurements was also made.

**Material.** A total of 297 children were investigated, 287 of these radiologically. The non-response was always due to the parents' fear of roentgen irradiation. The distribution according to age and sex is shown in Table 1.

The children were pupils at two comprehensive schools. They were judged to be healthy and to be of normal height. The parents represented a cross section of the town's distribution according to social grouping.

### Method

The roentgen films obtained consisted of a full-mouth set made up of two oblique-lateral extra-oral and four intra-oral films, three of the upper jaw, and one of the lower jaw as well as one film of each hand at a FFD of 70 cm and the palmar surface of the hand in contact with the film.



The developmental stages of teeth 0 = no calcified crown 0.5 = half the crown calcified 1 = the whole crown calcified no or only slight root 2 = completely visible root but shorter than the crown 3 = length of root about equal to the length of crown 4 = root longer than crown termination of root pointed 5 = root longer than crown termination of root rounded 6 = root development completed

*Assessment of the tooth development* The developmental stages of the tooth were divided into eight phases with numeric values from 0 to 6 according to the following scheme (see Figure) no calcified crown = 0, half the crown calcified = 0.5, the whole crown calcified, no or only slight root = 1, completely visible root but shorter than the crown = 2, length of root about equal to the length of crown = 3, root longer than crown, termination of root pointed = 4, root longer than crown termination of root rounded = 5, and root development completed = 6

The assessment was made for 3 + + 3 and 7 — — 7 The more complicated root anatomy in the upper jaw — premolar and molar — made the assessment uncertain and this was, accordingly, not investigated A mean value ( $\bar{x}$ ) and standard deviation (SD) were calculated for each tooth in every age-group according to the numeric values in the above scheme Furthermore a sum of 3 + 1 + and + 1 + 3 1 — 7 — and — 1 — 7 was computed for each child and from these sums the mean values and the standard deviation were then calculated

*Assessment of skeletal age* This was assessed in accordance with the principles indicated by SCHMID & MOLL, each bone in the wrist being measured in two directions at right angles to each other and referred to as breadth and height By height is meant the greatest length of the bone in a direction parallel with the corresponding phalanx The mean values and the standard deviation for height and breadth in every ossification centre were calculated Furthermore, the values for length and breadth were summated for each hand and from these the mean values and standard deviation were calculated for each age group

*Statistical analysis* This was done with automatic data processing at the data processing centre of Umeå University

Table 2

*Hand development Recordings for each child and each observer (sum of four measurements)*

| Child number | Observer |       |       |       |       | Total  | Mean | SD   |
|--------------|----------|-------|-------|-------|-------|--------|------|------|
|              | A        | B     | C     | D     | E     |        |      |      |
| 1            | 60.0     | 59.0  | 61.0  | 64.0  | 57.5  | 301.5  | 60.3 | 2.45 |
| 2            | 56.0     | 52.0  | 54.0  | 54.5  | 54.0  | 270.5  | 54.1 | 1.41 |
| 3            | 37.5     | 37.0  | 38.0  | 37.0  | 37.0  | 186.5  | 37.3 | 0.38 |
| 4            | 66.0     | 63.0  | 65.0  | 63.0  | 62.5  | 319.5  | 63.9 | 1.50 |
| 5            | 63.0     | 60.0  | 64.0  | 64.0  | 57.5  | 308.5  | 61.7 | 2.87 |
| 6            | 50.5     | 48.0  | 49.0  | 48.0  | 49.0  | 244.5  | 48.9 | 1.00 |
| 7            | 60.5     | 59.0  | 59.0  | 60.0  | 58.0  | 296.5  | 59.3 | 1.00 |
| 8            | 51.5     | 49.0  | 50.0  | 49.0  | 59.5  | 249.0  | 49.8 | 1.00 |
| 9            | 49.0     | 47.0  | 46.0  | 47.0  | 46.5  | 235.5  | 47.1 | 1.12 |
| 10           | 61.5     | 58.0  | 58.0  | 58.0  | 57.5  | 293.0  | 58.6 | 1.58 |
| 11           | 56.5     | 55.0  | 55.0  | 54.5  | 54.5  | 275.5  | 55.1 | 0.71 |
| 12           | 51.5     | 49.5  | 50.0  | 49.5  | 49.0  | 249.5  | 49.9 | 0.87 |
| 13           | 53.4     | 52.0  | 59.0  | 55.0  | 58.5  | 278.0  | 55.6 | 3.04 |
| 14           | 34.5     | 34.0  | 34.0  | 33.5  | 34.0  | 170.0  | 34.0 | 0.71 |
| 15           | 44.5     | 43.0  | 43.0  | 43.0  | 39.0  | 212.5  | 42.5 | 2.16 |
| Total        | 796.0    | 765.5 | 785.0 | 780.0 | 764.0 | 3890.5 |      |      |
| Mean         | 53.1     | 51.0  | 52.3  | 52.0  | 50.9  |        | 51.9 |      |
| SD           | 9.05     | 8.45  | 9.23  | 9.38  | 8.6   |        |      |      |

$$SD = \sqrt{\frac{\sum (x - \bar{x})^2}{n - 1}}$$

## Results

A method of investigation of this kind must, if to be of value, be repeatable with comparable results. Fifteen subjects were chosen at random from the material to find out the precision with which a recording of the development of the bones of the hand and the teeth could be repeated by other investigators. These formed the material for recordings by five investigators independently of one another. The height and breadth of two bones, viz. the hamatum and capitatum, were measured for the recording of the development of the bones of the hand. For the assessment of the tooth development—7 — 1 were recorded. The sum of the values obtained in the analysis was used in the statistical analysis (Tables 2 and 3). These tables indicate that the mean values per child deviate somewhat as between the different observers. However, this does not imply that there are systematic differences, i.e. differences recurring from child to child. A conventional analysis of variance was performed in order to ascertain whether the differences occurring between the observers were systematic and statistically significant.

Table 3

*Tooth development Recordings for each child and each observer (sum of value —1 —7)*

| Child number | Observer |      |      |      |      | Total | Mean | SD   |
|--------------|----------|------|------|------|------|-------|------|------|
|              | A        | B    | C    | D    | E    |       |      |      |
| 1            | 33       | 31   | 32   | 33   | 29   | 158   | 31.6 | 1.67 |
| 2            | 18       | 16   | 18   | 21   | 16   | 89    | 17.8 | 2.01 |
| 3            | 41       | 38   | 30   | 41   | 37   | 197   | 39.4 | 1.81 |
| 4            | 40       | 40   | 38   | 40   | 36   | 194   | 38.8 | 1.78 |
| 5            | 41       | 39   | 41   | 38   | 40   | 199   | 39.8 | 1.30 |
| 6            | 42       | 42   | 41   | 39   | 42   | 206   | 41.2 | 1.30 |
| 7            | 28       | 23   | 25   | 28   | 25   | 129   | 25.8 | 2.16 |
| 8            | 36       | 34   | 35   | 35   | 32   | 175   | 35.0 | 0.70 |
| 9            | 32       | 32   | 31   | 32   | 29   | 156   | 31.2 | 1.30 |
| 10           | 21       | 20   | 21   | 22   | 23   | 110   | 22.0 | 2.00 |
| 11           | 20       | 21   | 21   | 25   | 20   | 107   | 21.4 | 2.07 |
| 12           | 21       | 23   | 22   | 27   | 25   | 118   | 23.6 | 2.40 |
| 13           | 38       | 37   | 36   | 38   | 28   | 177   | 35.4 | 4.21 |
| 14           | 32       | 31   | 31   | 30   | 33   | 157   | 31.4 | 1.14 |
| 15           | 21       | 21   | 23   | 22   | 20   | 110   | 22.0 | 2.00 |
| Total        | 464      | 448  | 455  | 477  | 438  | 2287  |      |      |
| Mean         | 30.9     | 29.9 | 30.3 | 31.8 | 29.2 |       | 30.4 |      |
| SD           | 8.24     | 8.48 | 8.06 | 6.48 | 7.81 |       |      |      |

cant (Tables 4 and 5). The tables disclose small but significant differences between the observers as regards both the development of the bones of the hand and that of the teeth. This significance is lower, however, than that for the difference between the children.

The true variance between the children  $\sigma^2_{\text{child}}$  may be indicated by

$$\frac{\text{mean square for children} - \text{mean square for residuals}}{5}$$

while the true variance between the observers  $\sigma^2_{\text{observer}}$  is obtained by

$$\frac{\text{mean square for observers} - \text{mean square for residuals}}{15}$$

For the development of the bones of the hand this gives

$$\sigma^2_{\text{child}} = 78.27 \text{ and } \sigma^2_{\text{observer}} = 0.73$$



Table 4

*Hand development Analysis of variance based on data from Table 2*

| Source of variance | Degrees of freedom | Sum of squares | Mean of squares | F         |
|--------------------|--------------------|----------------|-----------------|-----------|
| Children           | 14                 | 5 507.00       | 393.35          | 197.66*** |
| Observers          | 4                  | 51.30          | 12.88           | 6.47***   |
| Residuals          | 56                 | 107.50         | 1.99            | —         |

Table 5

*Tooth development Analysis of variance based on data from Table 3*

| Source of variance | Degrees of freedom | Sum of squares | Mean of squares | F        |
|--------------------|--------------------|----------------|-----------------|----------|
| Children           | 14                 | 4 270.40       | 305.0           | 92.42*** |
| Observers          | 4                  | 58.65          | 14.7            | 4.45**   |
| Residuals          | 56                 | 182.30         | 3.3             | —        |

and for the tooth development

$$\sigma_{\text{child}}^2 = 60.3 \text{ and } \sigma_{\text{observer}}^2 = 0.76$$

The variance between the children is thus very much greater than that between the observers, which latter is, moreover, slight.

An investigation of this kind will indicate how and with what agreement the different observers group the children in reciprocal order. This grouping is presented in Tables 6 and 7.

Some idea of the agreement between the observers in their ranking of the children may be obtained by comparing the different observers in pairs with the help of Spearman's coefficient of rank correlation

$$r_s = 1 - \frac{6 \sum d^2}{n(n^2 - 1)}$$

The results of this comparison emerge from Tables 8 and 9, from which it appears that the correlation coefficients are at a high level.

The results reveal that both methods are well adapted for repeated and comparative investigations by different observers.

Table 6

*Hand development: The children ranked with regard to the recordings of each observer*

| Child number | Observer |       |       |       |       | Total |
|--------------|----------|-------|-------|-------|-------|-------|
|              | A        | B     | C     | D     | E     |       |
| 1            | 11 0     | 12 5  | 13 0  | 14 5  | 11 0  | 62 0  |
| 2            | 9 0      | 8 5   | 8 0   | 8 5   | 8 0   | 42 0  |
| 3            | 2 0      | 2 0   | 2 0   | 2 0   | 2 0   | 10 0  |
| 4            | 15 0     | 15 0  | 15 0  | 13 0  | 15 0  | 73 0  |
| 5            | 14 0     | 14 0  | 14 0  | 14 5  | 11 0  | 67 5  |
| 6            | 5 0      | 5 0   | 5 0   | 5 0   | 5 5   | 25 5  |
| 7            | 12 0     | 12 5  | 11 5  | 12 0  | 13 0  | 61 0  |
| 8            | 6 5      | 6 0   | 6 5   | 6 0   | 7 0   | 32 0  |
| 9            | 4 0      | 4 0   | 4 0   | 4 0   | 4 0   | 20 0  |
| 10           | 13 0     | 11 0  | 11 0  | 11 0  | 11 0  | 56 0  |
| 11           | 10 0     | 10 0  | 9 0   | 8 5   | 9 0   | 46 5  |
| 12           | 6 5      | 7 0   | 6 5   | 7 0   | 5 5   | 32 5  |
| 13           | 8 0      | 8 5   | 11 5  | 10 0  | 14 0  | 52 0  |
| 14           | 1 0      | 1 0   | 1 0   | 1 0   | 1 0   | 5 0   |
| 15           | 3 0      | 3 0   | 3 0   | 3 0   | 3 0   | 15 0  |
| Total        | 120 0    | 120 0 | 120 0 | 120 0 | 120 0 | 600 0 |

Table 7

*Tooth development: The children ranked with regard to the recordings of each observer*

| Child number | Observer |       |       |       |       | Total |
|--------------|----------|-------|-------|-------|-------|-------|
|              | A        | B     | C     | D     | E     |       |
| 1            | 9 0      | 7 5   | 9 0   | 9 0   | 8 5   | 43 0  |
| 2            | 1 0      | 1 0   | 1 0   | 1 0   | 1 0   | 5 0   |
| 3            | 13 5     | 12 0  | 13 0  | 15 0  | 13 0  | 66 5  |
| 4            | 12 0     | 14 0  | 12 0  | 14 0  | 12 0  | 64 0  |
| 5            | 13 5     | 13 0  | 14 5  | 11 5  | 14 0  | 66 5  |
| 6            | 15 0     | 15 0  | 14 5  | 13 0  | 15 0  | 72 5  |
| 7            | 6 0      | 5 5   | 6 9   | 6 0   | 5 5   | 29 0  |
| 8            | 10 0     | 10 0  | 10 0  | 10 0  | 11 0  | 51 0  |
| 9            | 7 5      | 9 0   | 7 5   | 8 0   | 8 5   | 40 5  |
| 10           | 4 0      | 2 0   | 2 5   | 3 0   | 4 0   | 15 5  |
| 11           | 2 0      | 3 5   | 2 5   | 3 0   | 2 5   | 13 5  |
| 12           | 4 0      | 5 5   | 4 0   | 5 0   | 5 5   | 24 0  |
| 13           | 11 0     | 11 0  | 11 0  | 11 5  | 7 0   | 51 5  |
| 14           | 7 5      | 7 5   | 7 5   | 7 5   | 10 0  | 39 5  |
| 15           | 4 0      | 3 5   | 5 0   | 3 0   | 2 5   | 18 0  |
| Total        | 120 0    | 120 0 | 120 0 | 120 0 | 120 0 | 600 0 |

Table 8

*Hand development Rank correlation between observers based on data from Table 6*

| Observer | A    | B    | C    | D    | E    |
|----------|------|------|------|------|------|
| A        | —    | 0.99 | 0.96 | 0.95 | 0.90 |
| B        | 0.99 | —    | 0.98 | 0.98 | 0.92 |
| C        | 0.96 | 0.98 | —    | 0.98 | 0.96 |
| D        | 0.95 | 0.98 | 0.98 | —    | 0.91 |
| E        | 0.90 | 0.92 | 0.96 | 0.91 | —    |

Table 9

*Tooth development Rank correlation between observers based on data from Table 7*

| Observer | A    | B    | C    | D    | E    |
|----------|------|------|------|------|------|
| A        | —    | 0.96 | 0.99 | 0.97 | 0.95 |
| B        | 0.96 | —    | 0.97 | 0.96 | 0.93 |
| C        | 0.99 | 0.97 | —    | 0.96 | 0.94 |
| D        | 0.97 | 0.96 | 0.96 | —    | 0.92 |
| E        | 0.95 | 0.93 | 0.94 | 0.92 | —    |

*Development of the methods* One of the aims of the investigation have been to simplify the methods as far as possible, above all by reducing the number of radiographic exposures and the number of recorded data. To this end a series of correlation tests have been performed.

A correlation test between the right and left hands indicated a strong bias as regards both the individual ossification centres and the sum total of all the values. The correlation factor  $r_{xy} = 0.98$  in both instances, where

$$r_{xy} = \frac{n\sum xy - \sum x \sum y}{\sqrt{n\sum x^2 - (\sum x)^2} \sqrt{n\sum y^2 - (\sum y)^2}}$$

A total of 22 measurements were made and recorded for one hand in an investigation of the development of the bones of the hand by the SCHMID & MOLL method. The number of these measurements should if possible be reduced.

A correlation test ( $r_{xy}$ ) between the height and breadth in the individual ossification centres reveals a varying but on the whole good agreement: capitate bone = 0.883, hamate bone = 0.907, radial epiphysis = 0.766, triquetral bone = 0.883, metatarsal bone = 0.787, lunate bone = 0.887, trapezium = 0.951, trapezoid bone = 0.938, scaphoid bone = 0.879, ulnar epiphysis = 0.864, and pisiform bone = 0.986. The lowest coefficient, 0.77, was obtained for the radial

Table 10

*Differences in breadth and height in the same child after one year (sum of totals) Age at first examination*

|                | 6 5—<br>7 5 | 7 5—<br>8 5 | 8 5—<br>9 5 | 9 5—<br>10 5 | 10 5—<br>11 5 | 11 5—<br>12 5 | 12 5—<br>13 5 | 13 5—<br>14 5 |
|----------------|-------------|-------------|-------------|--------------|---------------|---------------|---------------|---------------|
| <b>Breadth</b> |             |             |             |              |               |               |               |               |
| <b>Girls</b>   |             |             |             |              |               |               |               |               |
| Mean           | 11.8        | 13.2        | 15.2        | 15.3         | 13.7          | 13.5          | 5.4           | 4.6           |
| t value        | 12.4        | 21.2        | 9.6         | 12.0         | 12.2          | 6.4           | 3.6           | 3.1           |
| Significance   | ***         | ***         | ***         | ***          | ***           | ***           | **            | **            |
| <b>Boys</b>    |             |             |             |              |               |               |               |               |
| Mean           | 14.7        | 14.0        | 12.9        | 13.1         | 15.9          | 17.0          | 18.5          | 13.7          |
| t value        | 15.4        | 12.6        | 10.6        | 10.8         | 9.2           | 9.4           | 9.3           | 9.5           |
| Significance   | ***         | ***         | ***         | ***          | ***           | ***           | —             | —             |
| <b>Height</b>  |             |             |             |              |               |               |               |               |
| <b>Girls</b>   |             |             |             |              |               |               |               |               |
| Mean           | 10.2        | 10.2        | 15.0        | 11.3         | 12.3          | 11.1          | 0.6           | 0.8           |
| t value        | 13.4        | 21.2        | 10.1        | 8.9          | 7.7           | 5.1           | 0.5           | 0.6           |
| Significance   | ***         | ***         | ***         | ***          | ***           | ***           | —             | —             |
| <b>Boys</b>    |             |             |             |              |               |               |               |               |
| Mean           | 12.2        | 12.1        | 19.0        | 12.5         | 13.9          | 14.4          | 18.0          | 12.3          |
| t value        | 13.9        | 14.0        | 2.8         | 14.3         | 9.0           | 6.4           | 10.1          | 2.9           |
| Significance   | ***         | ***         | *           | ***          | ***           | ***           | ***           | *             |

epiphysis and the highest, 0.99, for the pisiform bone. A reduction in the number of measurements to 11 is thus possible. For statistical processing in connection with a comparison between large groups, however, the use of the individual values would imply an all too great accumulation of data. The possibility of using the sum of the 11 measurements may perhaps be possible provided that this sum indicates significant differences between the age groups. This point was investigated by recalling the 287 children first examined for a further examination thirteen months later but that time by the reduced method. A total of 270 children turned up for the examination. The non response, which was chiefly due to removals from the district and in one or two instances to fear of roentgen irradiation, was of no importance to the results. A t test was carried out for the differences between the sums for breadth and height in all age groups. Table 10 indicates that the differences for breadth are strongly significant, while those for height in two instances attain only \* significance. The sum totals for breadth seem well adapted for comparison between the groups.

A correlation test of tooth development between the right and left sides re-

Table 11

*Differences in tooth development in the same child after one year (sum of —1 —7) Age at first examination*

| Age group | Girls |         |      | Boys |         |      |
|-----------|-------|---------|------|------|---------|------|
|           | Mean  | t value | Sign | Mean | t value | Sign |
| 6.5—7.5   | 5.4   | 4.4     | ***  | 4.6  | 17.9    | ***  |
| 7.5—8.5   | 5.7   | 16.3    | ***  | 4.9  | 16.5    | ***  |
| 8.5—9.5   | 1.9   | 6.0     | ***  | 1.3  | 4.0     | **   |
| 9.5—10.5  | 3.0   | 6.3     | ***  | 3.5  | 6.5     | ***  |
| 10.5—11.5 | 1.0   | 3.2     | **   | 2.8  | 9.2     | ***  |
| 11.5—12.5 | 1.4   | 4.7     | ***  | 1.5  | 2.6     | *    |
| 12.5—13.5 | 0.3   | 1.7     | —    | 0.1  | 0.4     | —    |
| 13.5—14.5 | 0.9   | 2.9     | *    | 0.6  | 1.6     | —    |

reveals both for the individual tooth and for the sum of all values, a strong correlation,  $r_{xy} = 0.99$

A further reduction in the data recording may be made. A correlation analysis between the value totals +1 +3 and —1 —7 likewise produces almost complete agreement,  $r_{xy} = 0.99$ , the examination may thus be restricted to one jaw quadrant. For the sake of convenience one half of the lower jaw may be selected and implies the recording of seven data. As in connection with the examination of the bones of the hand, this would mean too many data in a comparison between large groups. A test of the sum totals was therefore made. Table 11 indicates that significant differences exist between the sum totals up to the age of 13.5 years. The sum totals are thus suited for comparison between groups aged between 6.5 and 13.5 years.

This investigation was intended to disclose whether any differences existing were so large as to necessitate special standards for girls and boys. Accordingly, a t-test was carried out with respect to the differences between the sums of the breadth measurements in the measurement of the bones of the hand and the sum for the tooth development —1 —7. Table 12 reveals that as regards the development of the bones of the hand the girls are significantly ahead of the boys up to the age of 12.5 years, that between 12.5 and 13.5 there are no differences, while after 13.5 the boys have a significant lead.

The differences are smaller as regards tooth development (Table 13). The girls are the whole time somewhat to the fore, but there are significant differences only in the age groups from 8.5 to 12.5 years. Thus special standards are needed for boys and girls respectively, above all as regards the development of the bones of the hand.

Table 12

*Differences in skeletal development (sum of totals for breadth) between sexes in the different age groups*

| Age group | Difference between girls and boys | t value | Sign |
|-----------|-----------------------------------|---------|------|
| 6.5—7.5   | 15.2                              | 3.04    | ***  |
| 7.5—8.5   | 13.3                              | 4.29    | ***  |
| 8.5—9.5   | 15.4                              | 4.51    | ***  |
| 9.5—10.5  | 19.0                              | 6.07    | ***  |
| 10.5—11.5 | 14.1                              | 4.66    | ***  |
| 11.5—12.5 | 9.6                               | 2.74    | **   |
| 12.5—13.5 | 4.3                               | 1.17    | —    |
| 13.5—14.5 | —9.0                              | 2.57    | *    |
| 14.5—15.5 | —18.2                             | 3.37    | **   |

Table 13

*Differences in tooth development (sum of totals for —1 —7) between sexes in the different age groups*

| Age group | Difference between girls and boys | t value | Sign |
|-----------|-----------------------------------|---------|------|
| 6.5—7.5   | 0.2                               | 0.2     | —    |
| 7.5—8.5   | 0.9                               | 1.91    | —    |
| 8.5—9.5   | 2.0                               | 2.85    | **   |
| 9.5—10.5  | 1.7                               | 2.83    | **   |
| 10.5—11.5 | 2.9                               | 4.83    | ***  |
| 11.5—12.5 | 2.1                               | 3.44    | ***  |
| 12.5—13.5 | 1.1                               | 1.83    | —    |
| 13.5—14.5 | 0.4                               | 1.09    | —    |
| 14.5—15.5 | 0.6                               | 1.09    | —    |

*Comparison between development of the bones of the hand and tooth development* A correlation analysis, covering all children between the sum of the breadth measurements and the tooth development —1 —7, indicates good agreement,  $r_{xy} = 0.88$

### Discussion

An important criterion of the correctness and reliability of a method is its reproducibility. It is natural to assume that measurements of distances should always give exactly or almost exactly the same result if these are performed by different observers. Where it is a matter of measurements in roentgen films of

Table 11

*Differences in tooth development in the same child after one year (sum of —1 —7) Age at first examination*

| Age group | Girls |         |      | Boys |         |      |
|-----------|-------|---------|------|------|---------|------|
|           | Mean  | t value | Sign | Mean | t value | Sign |
| 6.5—7.5   | 5.4   | 4.4     | ***  | 4.6  | 17.9    | ***  |
| 7.5—8.5   | 5.7   | 16.3    | ***  | 4.9  | 16.5    | ***  |
| 8.5—9.5   | 1.9   | 6.0     | ***  | 1.3  | 4.0     | **   |
| 9.5—10.5  | 3.0   | 6.3     | ***  | 3.5  | 6.5     | ***  |
| 10.5—11.5 | 1.0   | 3.2     | **   | 2.8  | 9.2     | ***  |
| 11.5—12.5 | 1.4   | 4.7     | ***  | 1.5  | 2.6     | *    |
| 12.5—13.5 | 0.3   | 1.7     | —    | 0.1  | 0.4     | —    |
| 13.5—14.5 | 0.9   | 2.9     | *    | 0.6  | 1.6     | —    |

veals both for the individual tooth and for the sum of all values, a strong correlation,  $r_{xy} = 0.99$

A further reduction in the data recording may be made. A correlation analysis between the value totals +1 +3 and —1 —7 likewise produces almost complete agreement,  $r_{xy} = 0.99$ , the examination may thus be restricted to one jaw quadrant. For the sake of convenience one half of the lower jaw may be selected and implies the recording of seven data. As in connection with the examination of the bones of the hand, this would mean too many data in a comparison between large groups. A test of the sum totals was therefore made. Table 11 indicates that significant differences exist between the sum totals up to the age of 13.5 years. The sum totals are thus suited for comparison between groups aged between 6.5 and 13.5 years.

This investigation was intended to disclose whether any differences existing were so large as to necessitate special standards for girls and boys. Accordingly, a t-test was carried out with respect to the differences between the sums of the breadth measurements in the measurement of the bones of the hand and the sum for the tooth development —1 —7. Table 12 reveals that as regards the development of the bones of the hand the girls are significantly ahead of the boys up to the age of 12.5 years, that between 12.5 and 13.5 there are no differences, while after 13.5 the boys have a significant lead.

The differences are smaller as regards tooth development (Table 13). The girls are the whole time somewhat to the fore, but there are significant differences only in the age groups from 8.5 to 12.5 years. Thus special standards are needed for boys and girls respectively, above all as regards the development of the bones of the hand.

Table 12

*Differences in skeletal development (sum of totals for breadth) between sexes in the different age groups*

| Age group | Difference between girls and boys | t value | Sign |
|-----------|-----------------------------------|---------|------|
| 6.5—7.5   | 15.2                              | 3.04    | ***  |
| 7.5—8.5   | 13.3                              | 4.29    | ***  |
| 8.5—9.5   | 15.4                              | 4.51    | ***  |
| 9.5—10.5  | 19.0                              | 6.07    | ***  |
| 10.5—11.5 | 14.1                              | 4.65    | ***  |
| 11.5—12.5 | 9.6                               | 2.74    | **   |
| 12.5—13.5 | 4.3                               | 1.17    | —    |
| 13.5—14.5 | —9.0                              | 2.57    | *    |
| 14.5—15.5 | —18.2                             | 3.37    | **   |

Table 13

*Differences in tooth development (sum of totals for —1 —7) between sexes in the different age groups*

| Age group | Difference between girls and boys | t-value | Sign |
|-----------|-----------------------------------|---------|------|
| 6.5—7.5   | 0.2                               | 0.2     | —    |
| 7.5—8.5   | 0.9                               | 1.91    | —    |
| 8.5—9.5   | 2.0                               | 2.83    | **   |
| 9.5—10.5  | 1.7                               | 2.83    | **   |
| 10.5—11.5 | 2.9                               | 4.83    | ***  |
| 11.5—12.5 | 2.1                               | 3.14    | ***  |
| 12.5—13.5 | 1.1                               | 1.83    | —    |
| 13.5—14.5 | 0.4                               | 1.09    | —    |
| 14.5—15.5 | 0.6                               | 1.09    | —    |

*Comparison between development of the bones of the hand and tooth development.* A correlation analysis, covering all children between the sum of the breadth measurements and the tooth development —1 —7, indicates good agreement,  $r_{xy} = 0.88$

### Discussion

An important criterion of the correctness and reliability of a method is its reproducibility. It is natural to assume that measurements of distances should always give exactly or almost exactly the same result if these are performed by different observers. Where it is a matter of measurements in roentgen films of



anatomic detail several sources of error must be taken into consideration. The general principles for the carrying out of the measurements may be so vaguely formulated that different investigators may choose different measuring points. Again, the measuring points are not always, even if correctly chosen, clearly identifiable in all films owing to slight variations in the normal anatomy or to a greater or lesser degree of geometric blurring of the image. The difficulties are obviously greater when instead of measuring distances it is necessary to indicate an organ by points. The practical value of the method will naturally be considerably reduced if the reliability is not such that the results arrived at by different investigators agree. The present investigation indicates that good agreement existed between the different observers as regards both the measurement of the wrist bones and the awarding of points for tooth development. The observers' ranking of the children also reveals satisfactorily high correlation coefficients. Both the investigations are thus well-suited for repeat and comparative examinations by different observers.

The investigation includes measurement of the wrist bones of both the left and right hands, as well as the awarding of points for tooth development in both the upper and lower jaws. Such comprehensive examinations are time-consuming and are therefore not suitable for practical use. In agreement with earlier investigations (GRFULICH & PIRF 1959) the correlation tests carried out disclose that no difference between the right and left hands exists. The correlation test also reveals that the method may be simplified without losing in precision by excluding the measurement of the length of individual bones. The rather time-consuming awarding of points for tooth development may also be made more simple by a restriction to the teeth in half of the lower jaw.

Most investigators are agreed that the process of maturing runs a different course in boys and girls and that standards must therefore be so adapted that boys and girls may be examined separately. SCHMID & MOLL stated however that no distinction should be drawn between boys and girls. SCHMID (1949) considered that the difference between the sexes was slight and referred in the main to the differentiation of the skeleton and, to a lesser extent, the development with respect to size and form. However, the present investigation has clearly indicated that above all in the assessment of the wrist bones, a clear difference between boys and girls existed. The difference is so considerable that special standards should be set up for boys and girls, it was less marked as regards tooth development, or though again it existed.

The literature contains only a few investigations of the correlation between the skeletal development assessed with reference to the ossification centres and tooth development. Most works appear to discuss the relation between skeletal age determined with the help of maturity indicators and the age of the teeth judged

in accordance with the total number of those erupted. The correlation is stated to be slight. This was not the case in the present investigation, in which a correlation analysis was carried out between the sum of the breadth measurements and the tooth development — 1 — 7. This appears to make it clear that the method of assessment of the degree of development of the teeth described affords a better measure of the degree of maturity of the subject than a recording of the number of erupted teeth.

### Conclusions

The aim of the investigation was fourfold: (1) to investigate the reliability of the method for determination of the skeletal age as used by SCHMID & MOLL, (2) to devise a method for determination of the tooth age by indicating numerical values, (3) to simplify the methods as far as possible, above all by reducing the number of roentgen exposures and the number of recorded data, and (4) to correlate these two methods to each other.

The results of these investigations indicate that both methods are very well adapted for repeated and comparative investigations by different observers. The determination of skeletal age can be carried out by use only of the breadth of the ossification centres and that the sum of these values is well adapted for comparison between groups. Tooth age may be obtained by the values of the teeth in one half of the lower jaw and that the sum of these values is well adapted for comparison between groups. Significant differences exist between boys and girls and that special standards are needed for these two groups.

The correlation between skeletal and tooth age determined by the methods described are very good.

### SUMMARY

The various methods of determining the physiologic age of a child are described. The investigation was directed at comparing the radiologic appearances of the skeleton and the tooth age. The correlation between these methods was very good. Significant differences were apparent between boys and girls.

### ZUSAMMENFASSUNG

Die verschiedenen Methoden, um das physiologische Alter eines Kindes zu bestimmen, werden beschrieben. Die Untersuchung war darauf gerichtet, das Skelett und das Bild des Zahnlalters zu vergleichen. Die Korrelation zwischen diesen beiden Methoden war sehr gut. Zwischen Jungen und Mädchen waren bedeutende Unterschiede zu beobachten.

## RÉSUMÉ

Les auteurs décrivent les diverses méthodes de détermination de l'âge physiologique de l'enfant. Leur travail a eu pour but de comparer les images radiologiques du squelette et l'âge dentaire. La corrélation entre les méthodes a été très bonne. Il y a des différences significatives entre les garçons et les filles.

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## PERCUTANEOUS BIOPSY OF VERTEBRAE AND RIBS

by

BJORN NORDENSTROM

Clinical and roentgenographic evidence of bone metastases is often sufficient to contra indicate operation in cases of malignancy. Attempts to arrive at a conclusive diagnosis must of course be made should the signs in the skeleton be in any way atypical. The facilities now available for localization of pathologic changes by roentgen television screening make possible the introduction of instruments for the sampling of material.

Tissue material was collected during videofluoroscopy in 17 patients with lesions thought to be vertebral metastases and in 17 patients with costal lesion. The technique is relatively simple and appears to be of considerable help in the establishment of a definite diagnosis.

*Vertebral biopsy with the Gidlund bone biopsy instrument.* The instrument (Kistner, Gothenburg, Sweden) is depicted in Figs 1 and 2. The indicator cannula (1) with winged nut (2) is attached to the handle (3) and introduced toward the biopsy region under local anesthesia. The cylindrical biopsy trephine with saw teeth (4 or 5) is then drawn on to the indicator cannula after removal of the handle (2, 3). When the trephine has reached the bone tissue, the pointed stylet (8) is introduced and the drill (13) attached. The bone tissue is then

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## RÉSUMÉ

Les auteurs décrivent les diverses méthodes de détermination de l'âge physiologique de l'enfant. Leur travail a eu pour but de comparer les images radiologiques du squelette et l'âge dentaire. La corrélation entre les méthodes a été très bonne. Il y a des différences significatives entre les garçons et les filles.

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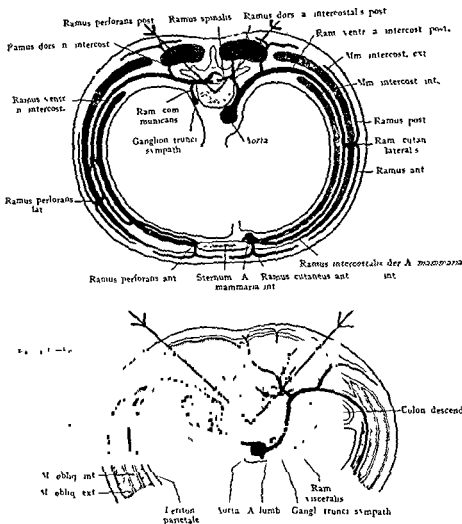


Fig 3 Transverse body sections of thoracic and lumbar regions (according to COVATTO) biopsy instrument has to be inserted into the vertebral bodies at an angle of up to  $45^\circ$  ag the sagittal plane, this angle is obtained during videofluoroscopy by turning the patient an oblique prone position

drilled to a pre-selected depth which is checked by videofluoroscopy and fi The pointed stylet is replaced by one of the solid metal rods (9, 10 or 11), rods are of different length so that the length of the biopsy samples may varied The depth of the cut made by the trephine is determined by the j tioning of the indicator ring (6) (Aspirations or injections through the trep

Fig 1 The Gidlund bone biopsy instrument 1) indicator cannula 2 3) handle with winged nut for indicator cannula 4 6) drill trephine with saw teeth and indicator ring 5 6) drill trephine with saw teeth and side hole for injection into bone tissue and indicator ring 7) Luer fitting adapter 8) sharp pointed stylet 9 10 11) blunt pointed stylets for 15 mm 30 mm and 90 mm long cores 12) stylet for removal of specimen 13) drill (reduced scale)

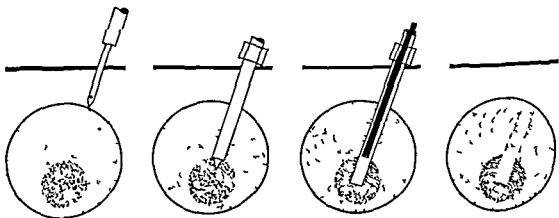
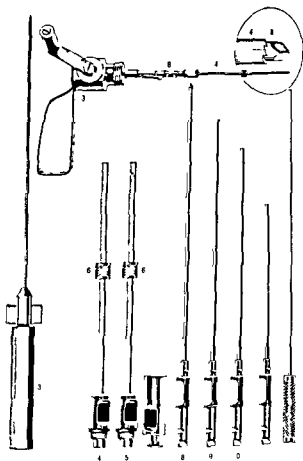


Fig 2 Principle of Gidlund bone biopsy

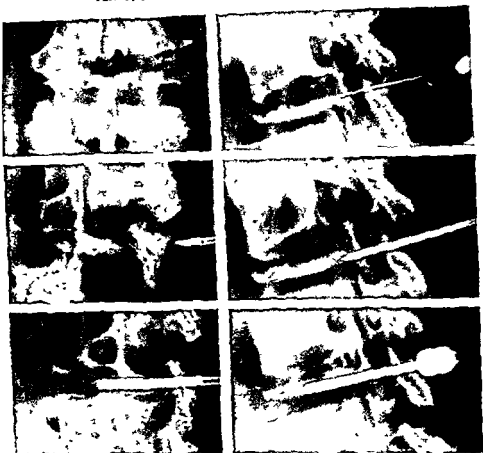


Fig 5 Biopsy from destroyed vertebral body of L3. The indicator cannula is introduced under biplane videofluoroscopy and then acts as a guide for the trephine which is drilled into the pathologic tissue (metastatic synovialoma).

may be made without the production of an artificial pneumothorax. The patient is turned into an oblique prone position during videofluoroscopy until the part of the vertebral body concerned is projected behind the pleura (Fig. 4).

Careful attention should be paid to the nerve roots in all regions of the spine. The instrument should have a relatively blunt point and should be advanced slowly with small rotational movements.

Biopsy of the body of a L3 vertebra is illustrated in Fig. 5, the positions of the anesthetic needle, guide stylet and trephine are depicted. The specimen removed contained tissue from a malignant synovialoma.

Vertebral biopsies were performed with the Gidlund instrument in 6 patients





Fig 4 Vertebral bodies between the ribs and posterior to the pleura (arrows) are easily accessed in a patient turned obliquely approximately  $45^\circ$  and with tube tilted  $30^\circ$  caudally

may be made by substituting the solid metal rod by a Luer fitting (7). The blunt rod with handle (12) is used for pushing out the bone specimen from the trephine.)

Two representative schematic thoracolumbar cross-sections are shown in Fig 3.

The introduction of the instrument is effected during videofluoroscopy in two perpendicular planes. After preparation of the skin the soft tissue is anesthetized with a fine needle introduced approximately 10 to 15 cm lateral to the mid line and directed about  $45^\circ$  to the sagittal plane. The indicator cannula is then introduced toward the posterior part of the vertebral body, which is systematically palpated from behind forward until the correct direction toward the biopsy region is found. More anesthetic may if necessary be injected through a fine needle into the lumen of the indicator cannula against the vertebral body. The procedure to obtain a core of tissue is continued as described. When the bone core has been removed it has often to be hammered out of the trephine with the blunt rod. The core is fixed in formalin, decalcified and further prepared for microscopy.

The nerve roots as well as the lung and pleura must be carefully avoided in biopsies in the thoracic regions. A simple way to preserve the lung surface intact is by the introduction of a moderate amount of air into the pleura before the biopsy. This, however, is not always necessary. Should the lesion be situated not too far anteriorly in the vertebral body direct insertion of the biopsy instrument



Fig 8 Tip of biopsy cannula with pointed stylet core of bone material and microscopy of material the latter revealed the presence of a metastatic bronchial carcinoma

region for biopsy has been reached, the stylet is withdrawn and the cannula is advanced for at least a further centimeter. The bone material is pushed out by means of a blunt stylet after the cannula has been removed.

The instrument inserted into a vertebral body is shown in Fig 7. The core of tissue, the size of the cannula tip and the microscopic appearances of a metastatic bronchial carcinoma are depicted in Fig 8.

Twelve vertebral biopsies were performed (L2, 3, 4 and Th5, 6, 6, 10, 11, 11, 12, 12). Metastatic structures were found in the material in 5 patients. A bone cyst was present in 1 patient and chronic inflammatory changes in 2 patients, no definite diagnosis was obtained in 4 patients. The pleura on the left side was pierced during a biopsy of Th6 from the left. The pneumothorax had to be aspirated. No other complications occurred.

Vertebral biopsy can be performed surprisingly easily with the fine, sharp cannula described, a satisfactory amount of bone tissue can be obtained to establish a diagnosis.

The pleural lesion occurred because of the selection of an unsuitable screening projection. A proper screening technique should eliminate such a complication.

*Biopsy of the ribs with the fine cannula.* The cannula described above has also been utilized for biopsies of rib lesions. These biopsies are, as in vertebral biopsies,

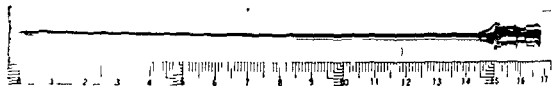


Fig 6 Sharp stainless steel cannula (18 mm) with pointed stylet for its introduction and blunt stylet for removal of the biopsy core



Fig 7 The cannula is introduced into the biopsy region and the stylet removed. The actual bone structure is entered by firm pressure upon and screwing movements of the instrument

(vertebral bodies L3, Th5, 6, 7, 9 and 11). Clinically and roentgenologically traumatic compression fractures were probably present in the 2 patients in whom normal tissue was obtained. The uncertainty about the etiology of the vertebral lesion was, however, partly due to the fact that both patients suffered from primary malignancy, metastatic tumour lesions were evident in 4 of the patients.

No complications were observed in connection with the biopsies.

In spite of rather limited experience it would appear that the Gidlund instrument is well suited for the biopsy of vertebral lesions in the lumbar and thoracic regions. It is easy to handle and bone samples of good size are obtained. Possible disadvantages of the instrument seem to be that the bone samples are sometimes unnecessarily large so that its use is limited in small patients and in the thoracic region.

*Vertebral biopsy by means of a simple sharp cannula.* The possibility of performing vertebral biopsies of the thoracic spine with removal of smaller samples than those obtained with the Gidlund instrument was tested in a series of 12 patients.

The instrument (Kifa, Stockholm, Sweden) is a simple 15 cm long, 18 mm wide sharp stainless steel cannula with a pointed stylet which is used during the insertion into the bone tissue (Fig 6). The introduction into the bone is made by manual rotation of the cannula under firm continuous pressure. When the

right eighth rib is seen in Fig. 9. The sample contained material from a moderately well differentiated squamous cell carcinoma.

Seventeen biopsies of ribs have been performed. There were no complications, such as local bleeding or damage to the pleura or lung. Malignant tissue was obtained in 7 patients, only inflammatory changes were found in 5 patients. Two osteomas and one bone cyst were discovered and in 2 patients the material contained only normal bone tissue.

### SUMMARY

A simple, relatively fine cannula has been tested for biopsy of lesions of the vertebral bodies in the thoracic and lumbar spines as well as for bone biopsy of lesions of the ribs under videofluoroscopic control. This would appear to possess advantages over the Gidlund instrument in certain cases.

### ZUSAMMENFASSUNG

Eine einfache, verhältnismässig dünne Kanüle zur Biopsie der Dorsal- und Lumbalwirbel und der Rippen unter Video-Röntgenkontrolle wurde auf ihre Zweckmässigkeit geprüft. Das Instrument scheint in gewissen Fällen dem Gidlund-Instrument überlegen zu sein.

### RÉSUMÉ

L'auteur a expérimenté un trocart simple, relativement fin, pour la biopsie des lésions des corps vertébraux dorsaux et lombaires ainsi que pour la biopsie des lésions costales sous contrôle radio-télévisé. Ce trocart paraît avoir des avantages sur l'instrumentation de Gidlund dans certains cas.

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Fig. 9 Biopsy of lesion of the eighth rib disclosed the presence of a moderately well differentiated squamous cell carcinoma.

performed under local anesthesia during videofluoroscopic control. The visual checking of the instrument makes it possible to reach the correct part of the pathologic process and to avoid damage of the underlying pleura and lung tissue. The position of the cannula at such a biopsy after the insertion into the

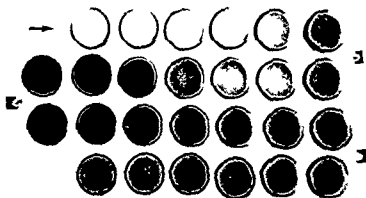


Fig 1 Roentgenogram of the bile samples

of contrast media by the oral intravenous and combined routes, (2) variations in the output of bile, and the concentration of the contrast medium it contains, following injection of bile acid

**Material and Methods** Twenty three experiments were made in three mongrel dogs weighing about 12 kg. The animals were cholecystectomized and provided with a permanent external common duct fistula. The interval between the creation of the fistula and the first administration of contrast medium exceeded four months. The dogs were re-fed with their bile together with a daily standard meal. They were in good general condition and the fistulas functioned well. Serum levels of bilirubin and alkaline phosphatase were controlled twice weekly and were normal throughout the investigation. The experiments were conducted in fasting animals every third day.

The contrast media and doses were Biligradin forte 50% for intravenous administration 0.6 ml/kg body weight and Solu Biloptin for oral administration 0.085 g/kg body weight. Apart from the dogs' apparently slight nausea on a few occasions, no side effects from the combined administration of contrast media by oral and intravenous routes were observed. The number of experiments in each dog are given in the Table and in Fig 2. The correlation between the bile output and the contrast concentration was investigated by the injection of bile acid (dehydrocholic acid), 0.03 g/kg body weight, and contrast medium intravenously separately and in combination (nine experiments in two dogs cf Figs 4, 5 and 6).

The bile was sampled in graded flat bottomed plastic tubes every 15 minutes for 3 to 4 hours and diluted with distilled water to equal volumes in one and

## INCREASED BILIARY CONCENTRATION OF CONTRAST MEDIA BY COMBINED ORAL AND INTRAVENOUS ADMINISTRATION

by

M. HAVERLING, J. SWEDENBORG and L. THULIN

Roentgen examination of the bile ducts after cholecystectomy is not invariably successful because of the often poor excretion of the contrast medium, even when no disturbance of liver function can be demonstrated. Theoretically, a combined oral and intravenous administration of contrast media should improve the radiographic demonstration of the ducts provided the two substances are excreted into the bile by different mechanisms. This approach has been recommended by PINOTTI & PONTES 1956, BETZLER & SCHMIDT 1958 and GOFERKE 1959. However, clinical assessments are subject to sources of error which make the results difficult to evaluate. It may for example be hard to achieve the same projection, identical exposure and the same general conditions for the patient on repeat examinations.

The present experimental investigation under standardized conditions was therefore instigated with a bile duct fistula in dogs by the well established technique of JONSON (1963). Two problems were dealt with: (1) the concentration of contrast medium in bile from the common duct on administration

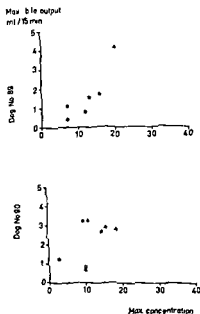


Fig 3 Correlation between maximum bile output and maximum biliary concentration of contrast medium injected intravenously

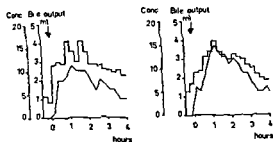


Fig 4 Bile output and biliary concentration of the contrast medium after intravenous administration in dog No 90 Upper curves indicate bile output lower curves concentration of the contrast medium

the same series of samples Roentgenograms of the samples were obtained by exposing the films, Gevaert Curix, to vertical rays at a film focus distance of 200 cm, 200 mA, 50 kV and 0.023 seconds (Fig 1) The roentgen ray absorption of contrast medium and bile was measured on the films with a densitometer (Macheth Quanta Log) The first two control samples, containing only bile, were taken as zero level The circular fields of the film were measured at four different spots, 1 mm<sup>2</sup> in size The differences between the measurement values of the spots the mean value The er significant



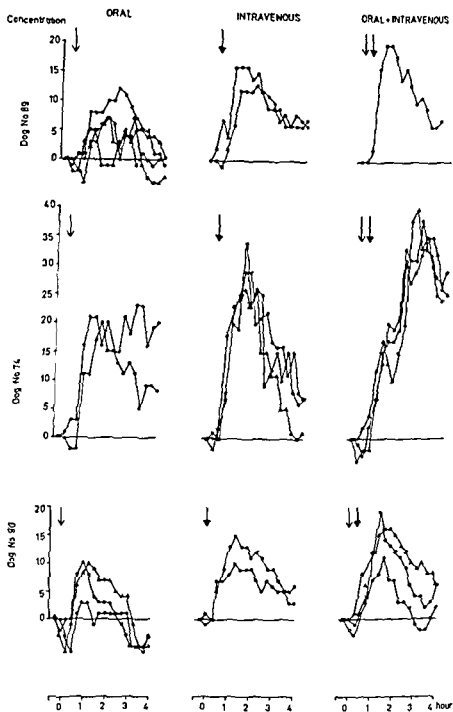


Fig 2 Biliary concentration of contrast media after oral intravenous and combined administration

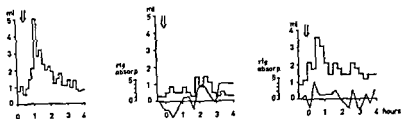


Fig 5 Bile output and roentgen ray absorption of bile after intravenous injection of bile acid (indicated by the arrows) in dog No 90 (left) dog No 108 (middle and right) Upper curves indicate bile output lower curves roentgen ray absorption of bile

necessary requirements for standardized conditions. An average of seven experiments were conducted in each dog, which thus served as its own control.

There appeared to be no signs of biliary obstruction in any of the animals, the levels of serum bilirubin and alkaline phosphatase being normal throughout the series. In addition, the excretion of contrast medium served as a measure of the hepatic function.

The prominent choleric effect of the contrast media was in direct relationship to the concentration of the latter in the bile. The effect may be explained in several ways, e.g. increase in hepatic blood flow, specific stimulation of the bile output or increased passive water output. The excretion of contrast medium was not enhanced by stimulating the choleresis with bile acid. This would suggest that the choleric effect could be ascribed to a passive water output secondary to the excretion of contrast medium, provided no competition existed between the bile acid and the contrast medium.

Little is known about the mechanism of excretion of contrast medium in the liver. A rival inhibition between orally and intravenously administered contrast media has been described (FINBY & BLASBERG 1964) but separate pathways are probably in general taken by such agents. The time of appearance of maximum

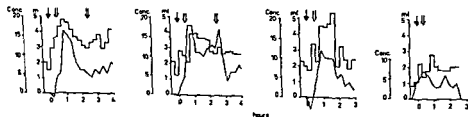


Fig 6 Bile output and biliary concentration of contrast medium (+) and bile acid (∩) in dog No 90 (left diagrams) and dog No 108 (right diagrams)

Table

*Number of experiments (n) and mean values of the maximum concentrations of the contrast media — The mean value after oral administration is indicated with 1*

| Dog | Method of administration |             |                       |
|-----|--------------------------|-------------|-----------------------|
|     | Oral                     | Intravenous | Intravenous plus oral |
| 89  | n = 4                    | n = 2       | n = 1                 |
|     | 1                        | 1 7         | 2 4                   |
| 74  | n = 2                    | n = 3       | n = 3                 |
|     | 1                        | 1 4         | 1 8                   |
| 90  | n = 3                    | n = 2       | n = 3                 |
|     | 1                        | 1 7         | 1 8                   |

## Results and Discussion

The biliary contrast medium concentration was higher after intravenous than after oral administration and was further increased on combination of both procedures (Table and Fig 2). The maximum concentration was reached 60 to 90 minutes after the oral administration and 15 minutes earlier after the intravenous injection. A 75% level of maximum concentration was maintained for about an hour. The biliary output rose up to three times its initial value with an increase in concentration of the contrast medium (Figs 3 and 4). Bile acid alone had its well-known choleretic effect but, as expected, did not influence the roentgen ray absorption of the bile (Fig 5). When bile acid was given together with contrast medium, the bile output was further increased although without appreciably affecting the biliary concentration of the contrast medium (Fig 6).

Failures in the radiographic examination of bile ducts may be due to several factors, e.g. deficient intestinal absorption of unusually high renal excretion of contrast medium, as well as impaired liver function, primary or secondary to biliary obstruction. For these reasons it is impossible to make even a rough estimate of the concentration of contrast medium in the bile ducts in ordinary cholegraphies. Standardized films of bile samples containing the excreted contrast medium would appear to be advantageous. An examination of samples of bile from patients supplied with temporary bile duct fistulas after choledochotomy would then of course be necessary, an approach that would hardly be acceptable. Since there is no evidence that the mode of excretion of contrast media by the liver differs in man and dog, bile duct fistulas experimentally applied in the animal by the technique of JONSON (1963) would seem to fulfill the

## IOGLYCAMIDE (BILIVISTAN) AS A CONTRAST MEDIUM FOR INTRAVENOUS CHOLEGRAPHY

A clinical and experimental investigation

by

J BRISMAR, P LINDGREN and G F SALTZMAN

Iodipamide (Biligradin, Chologradin) has been the only usable contrast medium for intravenous cholegraphy since it was introduced at the beginning of the 1930s. Although it has greatly improved diagnostic resources, its side effects have presented considerable problems. Since preparations of the acetate type were given up in angiographic and urographic work iodipamide has been the most toxic of all the parenterally administered contrast media. While the classical hypersensitivity reactions with urticaria as the commonest, have also been far from rare, it is the circulatory side effects that have caused the most serious problems. A fall in blood pressure is a constant phenomenon in connection with intravenous injection, it may vary, but may sometimes be highly dangerous (FROMMHOFF & BRABAND 1960, SALTZMAN & SUNDBSTROM 1960, LINDGREN & SALTZMAN 1962, LINDGREN et coll 1964). Any attempt to produce a preparation having lower toxicity but with equally good diagnostic properties must therefore be hailed with interest. Peroral cholegraphy has

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concentration of each medium is then the limiting factor for its accumulation in the bile. The dosages in this investigation were kept high in an effort to guarantee that excess contrast medium for excretion was available. The accompanying Table and Fig. 2 indicate that the levels reached by contrast media in the bile are not simply additive, this suggests that the two substances are excreted by separate mechanism which, however, may have some factor in common.

In contrast to the experiences of FINBY & BLASBERG in cholecystectomized human subjects the present experimental investigation supports the impressions of PINOTTI & PONTES, of BETZLER & SCHMIDT and GOERKE that a combined administration of contrast media by both oral and intravenous routes would be of benefit in roentgen examinations of the biliary tract both before and after operation.

## SUMMARY

The concentration of contrast medium in the bile in cholecystectomized dogs with permanent biliary fistula proved to be higher after intravenous than after oral administration and was further enhanced by a combination of both procedures. Twenty three experiments in 3 dogs are discussed.

## ZUSAMMENFASSUNG

Die Konzentration von Kontrastmittel in der Galle in Hunden mit permanenten Gallen fisteln war höher nach intravenöser als nach oraler Verabreichung und war noch höher wenn beide Methoden kombiniert wurden. Dreiundzwanzig Versuche in drei Hunden werden diskutiert.

## RÉSUMÉ

Chez les chiens cholecystectomisés et porteurs d'une fistule biliaire permanente la concentration du moyen de contraste dans la bile est plus élevée après administration intraveineuse qu'après administration orale et est encore augmentée par l'association de ces deux voies. Les auteurs examinent vingt trois expériences sur 3 chiens.

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Films were taken at intervals of 15 minutes following the injection. As soon as contrast medium became visible in the bile ducts, morphine was administered subcutaneously in a dose of 0.1 ml of a 1% solution per 10 kg bodyweight and followed by tomography 10 to 15 minutes later. When it was considered that the ducts had been satisfactorily examined the morphine induced contraction of the sphincter was stopped by the intramuscular injection of 2 ml of Cetiprin (Recip).

Oral cholecystography with Biloptin (Schering) as the contrast medium was also performed in 179 of these 500 cases.

The serum bilirubin was determined in direct connection with the cholegraphy, usually before the examination. No bilirubin determination was carried out in a few out patient cases without clinical icterus.

A total of 194 of the 500 cases had undergone cholecystectomy and 306 still had intact gallbladders. In the latter cases films were taken until the gallbladder was filled with contrast medium (up to 4 hours).

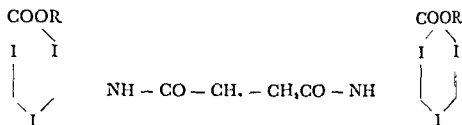
Any side effects that occurred in connection with the cholegraphy were recorded. The concentration of contrast medium in the biliary tract was assessed and graded into one of three groups: diagnostically adequate, poor definition, or no definition. The contrast density in the gallbladder was assessed as well, in the non cholecystectomized cases and was compared roughly with the density obtained at oral cholecystography in those cases in which this examination had been performed.

*Experimental investigations.* The circulatory effects of Bilivistan and Biligrafin forte, injected intravenously and intra arterially, were investigated in 12 cats anaesthetized by intraperitoneal injection of pentothal sodium (30 to 40 mg/kg). All the cats were tracheotomized. Heparin was given intravenously (25 mg/kg) in order to avoid coagulation.

The arterial blood pressure was recorded in the carotid artery with a Statham electromanometer (p 223 AA) connected to a Grass polygraph, model 7. In those cats in which the pressure in the right ventricle was recorded, a narrow polyethylene catheter was inserted through the right jugular vein and connected to another Statham transducer. The peripheral circulation was recorded with the photoelectric dropchamber technique described by LINDGREN (1958) and GOLDSCHMIDT & LINDGREN (1962). The intravenous injections were given through a fine polyethylene catheter inserted into a superficial vein in one of the forelegs, and the intra arterial injections through a side tube on the out going tube from the dropchamber.

The contrast media used were the ordinary, commercially available preparations of adipiodon (iodipamide) (Biligrafin forte 50%) and ioglycamide (Bilivistan 50%).

been described as an alternative (GUNNARSSON 1959, SALTZMAN 1959, VIRTAMA 1959, and others), but this technique involves great practical difficulties for roentgen units with a heavy load of work. Schering AG have now introduced a new contrast medium for intravenous cholegraphy. The new medium is a mixture of the sodium salt and the methylglucamine salt of ioglycamine and is sold under the trade name of Bilivistan. It has the formula



Several papers dealing with Bilivistan have already been published, most of them have described clinical trials, but some include experimental investigations. The optimal excretion from the liver takes place over a longer period than with Biligradin. This is considered one of the great advantages of Bilivistan (HORPE 1964, HAASSTERT 1964), as this allows a longer time for obtaining films with maximum contrast density in the biliary tract. Bilivistan has a slightly higher iodine concentration than Biligradin, but this is apparently offset by a slightly higher renal excretion. Opinions differ regarding the side effects. Whereas some authors consider them to be less severe (SCHIRMEISEN 1964, KRAMER 1964, FRIK & CFN 1964, BELL & BRABAND 1966, WILBRAND & ARTURSON 1968), others have observed no definite differences (HAASSTERT). Experimental investigations at the manufacturer's research laboratories have indicated that Bilivistan has a less marked depressant effect on blood pressure than Biligradin (LANGECKER et coll 1964, KRAMER 1964). The LD<sub>50</sub> dose is much higher for Bilivistan than for Biligradin in mice, rats and dogs (LANGECKER et coll). No investigators have been willing to state that Bilivistan causes more severe side reactions than Biligradin.

### Material and Methods

*Clinical trials* Five hundred consecutive cases examined by cholegraphy with Bilivistan as the contrast medium were investigated. Except in a few cases which will be discussed further on, 20 ml of Bilivistan were administered by intravenous injection within 4 to 5 minutes. In a few cases the injection speed was more rapid, but was never greater than 15 minutes. As these cases presented no differences from the others with respect to side effects or other reactions, the material will be treated as a whole in this investigation.

Three cases with liver damage after long use of oral contraceptives form a special group. These have been included in another material to be treated in a separate paper (LINDGREN et coll., to be published).

There are thus 4 cases in which a reasonable explanation of why the bile ducts failed to fill was not obtained. For an evaluation of the diagnostic values of a contrast medium to be meaningful, it would seem logical to discard all cases in which, for various reasons, weak contrast density or no visible contrast medium within the ducts can be expected in advance. The tabulation given below may therefore be considered to give a better representation of the actual quality of the contrast medium from the aspect of a diagnostically adequate concentration in the biliary tract.

|                         |     |          |
|-------------------------|-----|----------|
| Diagnostically adequate | 442 | (96.7 %) |
| Poor definition         | 11  | (2.4 %)  |
| No definition           | 4   | (0.9 %)  |
| Total                   | 457 | (100 %)  |

This indicates that Bilivistan provides excellent conditions for adequate diagnosis. As no case by case comparisons with Biligrafin were made, the figures do not permit an accurate comparison, but there seems every justification for saying that Bilivistan offers diagnostic possibilities equally as good as, if not better than those offered by Biligrafin.

It should be mentioned that with the exception of the case with weak concentration of contrast medium in the bile ducts when the bilirubin value was 2.2 mg per 100 ml, no filling of the ducts in any case with a bilirubin value over 2 mg was ever observed.

*Side effects.* Side reactions have been treated in different ways by different investigators. Taste sensations and a feeling of warmth were not classed as side reactions, as these phenomena are usually not mentioned by a patient except in response to a direct question and there is always the risk that the power of suggestion may elicit a positive answer.

The side effects were divided into two groups: symptoms that were not present before the examination (unquestionable side effects), and sensations that were experienced during the examination but were also reported before it was begun. The reason for this grouping was that the material is probably not fully comparable with most of the other cholegraphy materials, since cholegraphy has been used to a considerable extent in acute abdominal cases in which nausea and vomiting are common symptoms.

The side effects in the material are given in Table 1.

The case with circulatory collapse needs to be more fully discussed. This



The kidneys from cats that had received Bilivistan in a large clinical dose by rapid intravenous injection were subjected to histologic examination (C. M. Fajers).

## Results

### *Clinical trials*

*Contrast density in the biliary tract* On the basis of the rough system of classification described above, the material fell into the following groups

|                         |     |          |
|-------------------------|-----|----------|
| Diagnostically adequate | 142 | (88.4 %) |
| Poor definition         | 19  | (3.8 %)  |
| No definition           | 39  | (7.8 %)  |
| Total                   | 500 | (100 %)  |

This in itself indicates a high frequency of diagnostically adequate contrast concentration. If the cases with poor or no definition of the bile ducts are examined in more detail however a more correct idea of the situation will be obtained.

Of the 19 cases with poor concentration in the ducts 2 had bilirubin values of 2.2 and 1.9 mg per 100 ml, respectively. In 2 cases with normal bilirubin values, the examinations were carried out on the day when these values returned to normal after an attack of icterus with daily bilirubin controls. In one case with a normal bilirubin value, this had risen the following morning to 2.3 mg, and in another, a stone in the choledochous duct was diagnosed. In a further 2 cases, only 6 and 10 ml of contrast medium had been injected owing to secondary reactions. There remain 11 cases in which no satisfactory explanation of the poor contrast filling could be found, disease of the biliary tract or pancreas was diagnosed later in 7 of these cases however.

In 16 of the 39 cases without signs of contrast medium in the bile ducts a bilirubin value of over 2 mg per 100 ml was established. In 2 cases the bilirubin value was 1.9 mg, in 1 case with a value of 1.7 mg there was a stone in the choledochous duct, and in 1 case with a value of 1.4 mg immediately before the examination it was 2.5 mg next morning. The cholegraphy was performed during a phase of rapidly rising bilirubin values in a further 3 cases, values of over 2 mg were however not reached until 2 to 3 days after the cholegraphy. In 2 cases with bilirubin values of 1.3 and 1.0 mg, respectively, the patients had icterus a few days before, and a further fall in the values was noted after the cholegraphy. Only 1 to 3 ml of Bilivistan were injected in 3 cases because of side effects. One case had had a choledochoduodenostomy, and in 3 others extensive liver resection had been performed before the cholegraphic examination.

Table 3  
*Frequency of side effects by sex*

|                                  | Men        | Women     |
|----------------------------------|------------|-----------|
| Number of cases                  | 149        | 351       |
| Unquestionable side effects      | 15 (10.1%) | 34 (9.7%) |
| Same symptoms before examination | 9 (6.1%)   | 31 (8.8%) |

Table 4  
*Frequency of side effects in relation to cholecystectomy*

|                                  | Non cholecystectomized cases | Cholecystectomized cases |
|----------------------------------|------------------------------|--------------------------|
| Number of cases                  | 306                          | 194                      |
| Unquestionable side effects      | 31 (10.1%)                   | 18 (9.3%)                |
| Same symptoms before examination | 28 (9.2%)                    | 12 (6.2%)                |

(LINDGREN et coll., to be published). Thus, it would appear that side effects resulting from Bilivistan were not particularly frequent. Severe reactions were rare, but the very fact that a few did occur means that the use of Bilivistan does not eliminate the risk of such complications. Although the definite impression exists that the incidence of side effects has decreased noticeably since Biligrafin was replaced by Bilivistan no attempt at scientific comparisons will be made. When large series of cases from a time-consuming examination like cholegraphy are being assembled, shifts in the indications are likely to occur, making the materials difficult to compare. A large number of acute abdominal cases were included in the present series (BECKER et coll. 1970). The observations suggest that the increasing use of oral contraceptives may be affecting the incidence of side effects (LINDGREN et coll.). Two examples of circumstances that could have affected this material more than earlier series have been mentioned.

Cholecystectomized cases were compared with non-cholecystectomized cases to throw light on how acute abdominal cases can influence the frequency of side effects (Table 4).

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hospital (Table 5). The acute abdominal condition was usually acute cholecystitis.

Table 1

*Side effects in the present material*

|                                  | Nausea | Vomiting | Circulatory collapse | Urticaria | Urticaria, nausea | Irritative cough | Total      |
|----------------------------------|--------|----------|----------------------|-----------|-------------------|------------------|------------|
| No symptoms before examination   | 17     | 13       | 1                    | 12        | 5                 | 1                | 49 (98 %)  |
| Same symptoms before examination | 24     | 16       | —                    | —         | —                 | —                | 40 (80 %)  |
| Total                            | 41     | 29       | 1                    | 12        | 5                 | 1                | 89 (178 %) |

Table 2

*Frequency of side effects by age*

|                                  | 0—40 years  | 40—60 years | > 60 years |
|----------------------------------|-------------|-------------|------------|
| Number of cases                  | 110         | 205         | 185        |
| Unquestionable side effects      | 14 (12.7 %) | 24 (11.7 %) | 9 (4.9 %)  |
| Same symptoms before examination | 13 (11.8 %) | 19 (9.3 %)  | 10 (5.4 %) |

patient, a woman aged 56, was examined during the acute stage of her illness which was later interpreted as typical acute pancreatitis. Roentgen examinations indicated that she had arteriosclerosis that could be described as advanced for her age as well as severe pulmonary emphysema. At the completion of the injection (5 minutes) she had nausea and vomited, broke out in a cold sweat, and became pale and temporarily pulseless. She lost consciousness for 15 minutes. After one hour, she had recovered completely and the examination could be continued.

The incidence of side effects decreased with increasing age, in the same way as after the administration of Biligradin (SALTZMAN 1959). The distribution appears in Table 2.

A comparison between all men and women in the material brought out no definite sex differences (Table 3).

The age and sex distributions do not provide complete information with this rough system of grouping however. A more differentiated classification has been carried out in another connection and has revealed some interesting aspects

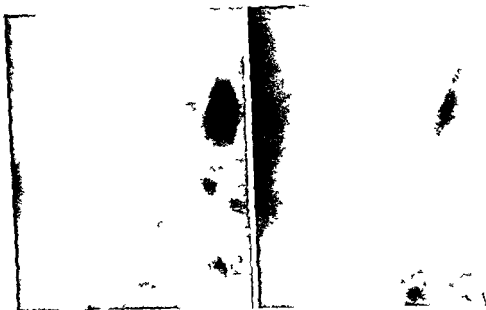


Fig 1 Layering in the gallbladder suggestive of gallstone Cholangiography with Bilivstan Operation revealed no gallstones

The high incidence of side effects appears in itself a definite *contraindication* to the use of cholegraphy when the gallbladder alone is to be examined. This view is also valid when Bilivstan is to be employed since the risk of circulatory collapse has not been wholly eliminated. One or two observations seem worth mentioning as a further commentary on this question.

Bilivstan like Biligrafin often produces layering between contrast bearing and non-contrast bearing bile in the gallbladder. This phenomenon has been described by FRIK & CEN. Such layering often makes the diagnosis of gallstone extremely difficult or

The case in Fig 1 of the high incidence of the layering phenomenon. Operation immediately after the cholegraphic examination proved the gallbladder to contain no concretions. Layering in the gallbladder may usually be eliminated by administering an agent with contractile action on the gallbladder. This prolongs the examination however.

Intravenous cholegraphy with Bilivstan and peroral cholecystography with Bilopon were performed in the same case in 179 instances. Although comparisons present certain difficulties because the examinations could not be carried out in close succession the observations nevertheless may be of some interest.

Table 5

*Frequency of side effects in acute abdominal cases*

|                                  | Acute abdominal cases | Other cases |
|----------------------------------|-----------------------|-------------|
| Number of cases                  | 102                   | 398         |
| Unquestionable side effects      | 10 (9.8%)             | 39 (9.8%)   |
| Same symptoms before examination | 17 (16.7%)            | 23 (5.8%)   |

Tables 4 and 5 demonstrate how the composition of the material can affect the frequency of side reactions. The acute abdominal cases in the material failed to influence the incidence of unquestionable side effects, in other words the symptoms not present before the cholecystography. On the other hand there were a considerable number of acute abdominal cases with nausea and vomiting during the cholecystography to the same extent as before the examination. This suggests that in the latter cases most of the symptoms could not be regarded as reactions due to the contrast medium. A comparison between Tables 4 and 5 reveals the risks involved in uncritically comparing two parts of a material. Table 4 could easily lead to the conclusion that the incidence of side effects decreases after cholecystectomy. In actual fact however the whole decrease demonstrated arose because the acute abdominal cases occurred in that part of the material in which the patients had not undergone cholecystectomy.

Earlier papers dealing with side reactions after the use of Biligrafin have mentioned the remarkable observation that side reactions were not seen in jaundiced patients (LIEFANDER 1955, SALTZMAN 1959 and others). In the present material there were 17 patients with serum bilirubin values exceeding 2 mg per 100 ml. Unquestionable side effects were not observed in a single one of these cases. It is true that in three instances nausea was noted during the examination but the same symptoms had been present before the cholecystography.

*Filling of the gallbladder.* Peroral cholecystography has long been the method of choice for roentgen examination of the gallbladder. In recent years however many investigators have recommended the use of intravenous cholecystography as the standard method of examination not only for the bile ducts but also for the gallbladder. The reason for this recommendation is that cholecystography offers the possibility of demonstrating the gallbladder in cases where this cannot be achieved with peroral cholecystography. Intravenous cholecystography is probably today the only method used in many hospitals for roentgen examinations of the biliary tract.

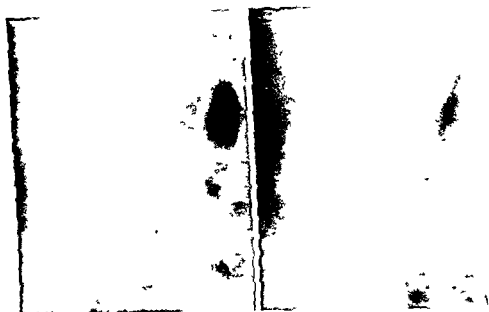


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Bilivistan, like Biligrafin, often produces layering between contrast bearing and non contrast bearing bile in the gallbladder. This phenomenon has been described by FRANK & CEN. Such layering often makes the diagnosis of gallstone extremely difficult or even impossible. Figs 1 to 3 represent such cases.

The case in Fig 1 was diagnosed as *cholecystitis with full knowledge* of the high incidence of the layering phenomenon. Operation immediately after the cholegraphic examination proved the gallbladder to contain no concretions. Layering in the gallbladder may usually be eliminated by administering an agent with contractile action on the gallbladder. This prolongs the examination however.

Intravenous cholegraphy with Bilivistan and peroral cholecystography with Bilopon were performed in the same case in 179 instances. Although comparisons present certain difficulties because the examinations could not be carried out in close succession, the observations nevertheless may be of some interest.

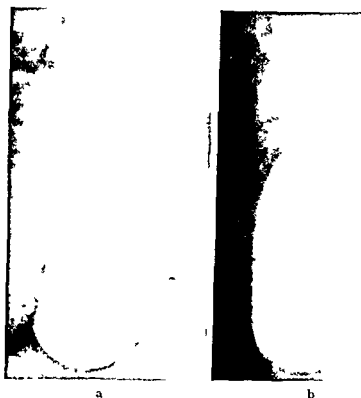


Fig. 2 a) Homogeneous filling of the gallbladder. Oral cholecystography b) Three weeks later. Layering after cholecystography with Bilivistan

The filling of the gallbladder was similar, both with cholecystography and with cholecystography, in 145 cases (82 %). In the remaining 34 cases (18 %) the contrast density in the gallbladder was considerably different in the two examinations, a higher density was noted in 19 cases examined by cholecystography and in 15 by cholecystography. To permit a meaningful comparison all cases with icterus at the one examination but not at the other must be excluded. When this had been done, there remained 11 cases in each group. No evidence was thus obtained to confirm that intravenous cholecystography could provide better cholecystography, at least not when Bilivistan and Biloptin were used.

In summary, oral cholecystography appears on the whole the method of choice for examination of the gallbladder. Intravenous cholecystography is contra indicated because of the higher frequency of side effects and a troublesome layering phenomenon. There seems to be no evidence that cholecystography gives a higher concentration of contrast medium in the gallbladder.

There are two situations however in which the use of intravenous cholecystography is indicated for examination of the gallbladder, that is to say acute abdominal

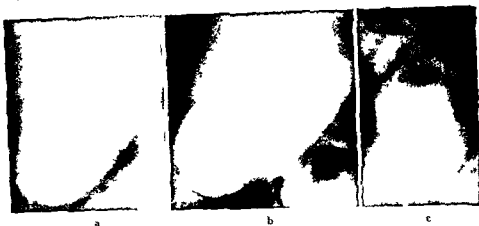


FIG. 3. Layering of contrast medium in the gallbladder after cholecystography with Bilivistan (b). Homogeneous filling after oral cholecystography both before (a) and after (c) cholecystography.

cases in which operation is being considered and acute cholecystitis is a differential alternative (BECKER et coll., and others). Cholecystography is indicated in these cases for time saving reasons, (as compared with oral cholecystography) and is only intended as a measure to find out whether the gallbladder fills or not. It is obvious, on the other hand, that obstruction to the passage and resorption in the alimentary tract often means that cholecystography is the only possible method for roentgen examination of the gallbladder.

### Experimental investigations

*Circulatory effects after intravenous injections.* A fall in blood pressure was observed after the rapid intravenous injection of Biligradin forte as in earlier investigations (LINDGREN & SALTZMAN 1962). A characteristic experiment is illustrated in Fig. 4. A dose of 0.67 ml/kg caused a fall in the mean arterial pressure from 100 to about 60 mm Hg and the reaction lasted for roughly 5 minutes. The same dose of Bilivistan caused a much smaller reaction, with a pressure fall from 90 to 75 mm Hg.

The object of these investigations was not only to investigate the effects of Bilivistan as such, but also and not least, to compare them with the effects produced by Biligradin forte. In such a comparison, consideration must be paid to the tachyphylaxis that has previously been observed (LINDGREN & SALTZMAN) in connection with the use of Biligradin forte. According to this observation, repeated intravenous injections of Biligradin forte produce decreasing blood pressure falls after each new injection. The question arises as to whether any



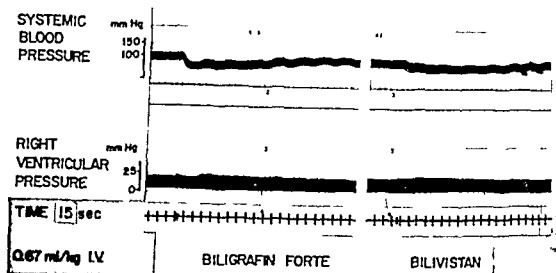


Fig. 4 Effect of intravenous injections (0.67 ml/kg) of Biligradin forte and Bilivistan on arterial blood pressure and right ventricle pressure

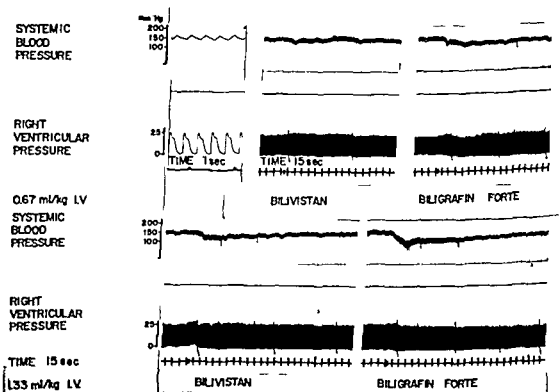


Fig. 5 Effect of intravenous injections (top 0.67 ml/kg bottom 1.33 ml/kg) of Bilivistan and Biligradin forte on arterial blood pressure and right ventricle pressure. The contrast media were injected in the opposite order to that in which they were given in fig. 4

cross tachyphylaxis between Biligrafin forte and Bilivistan exists. In order to exclude the possibility that such a phenomenon could be the reason for the different effects that were recorded in experiments of the type shown in Fig. 4, the order of the injections was altered in a few experiments. Biligrafin forte still had a stronger effect in spite of the altered order (Fig. 5). This was particularly noticeable when a double dose (1.33 ml/kg) was given. This result — that Biligrafin forte caused a larger fall in blood pressure than Bilivistan after intravenous injection — was consistently found in this series of experiments, irrespective of the reciprocal order in which the two preparations were injected. Thus, any possible cross-tachyphylaxis between the two media is not strong enough to prevent a later Biligrafin forte injection from producing a larger blood pressure fall than a preceding Bilivistan injection.

Both Biligrafin forte and Bilivistan produced relatively small changes in the right ventricle pressure in the experiments illustrated (Figs 4 and 5). A slight rise was noted however after the first injection in the respective experiments. It is known from earlier investigations (LINDGREN *et coll.*) that the reaction in right ventricle pressure rapidly produces tachyphylaxis in response to repeated injections. The changes were too small for definite conclusions to be drawn regarding possible differences between the two contrast media in this respect.

The peripheral blood flow was recorded in a few experiments after intravenous injections of contrast medium (Fig. 6). The changes were of the type previously described for Biligrafin forte (LINDGREN & SALTZMAN), in other words a small decrease in the flow rate concurrently with the fall in blood pressure. As mentioned above Bilivistan caused a smaller blood pressure fall than Biligrafin forte, and probably as a consequence of this, only a very slight decrease in the flow was observed after the Bilivistan injection (Fig. 6).

*Vascular effects after intra arterial injections.* It has been demonstrated in several earlier publications (LINDGREN & TORNELL, LINDGREN & SALTZMAN), that intra arterial administration is more suitable for comparative studies of the immediate vascular effects of different contrast media than intravenous injections. Smaller doses can be injected, and consequently the animals can be used for experiments lasting for a longer period. Although smaller doses are used, the contrast concentration in the vessel under examination will be higher than after the intravenous injection of much larger doses. Changes in the vasomotor tonus due to reflex action are also lessened. In view of these observations, the effects of intra arterial injections of Bilivistan and Biligrafin forte were compared, despite the fact that this form of administration is not practised with these contrast media in clinical work.

A few cats were given increasing doses of Bilivistan in order to investigate the

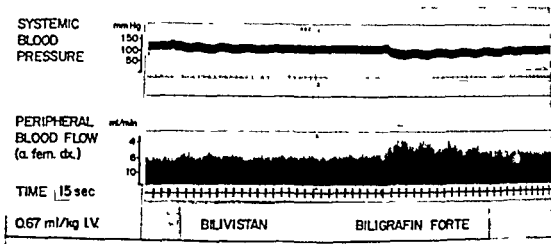


Fig 6 Effect of intravenous injections (0.67 ml/kg) of Bilivistan and Biligrafin forte on arterial blood pressure and the flow in the femoral artery.

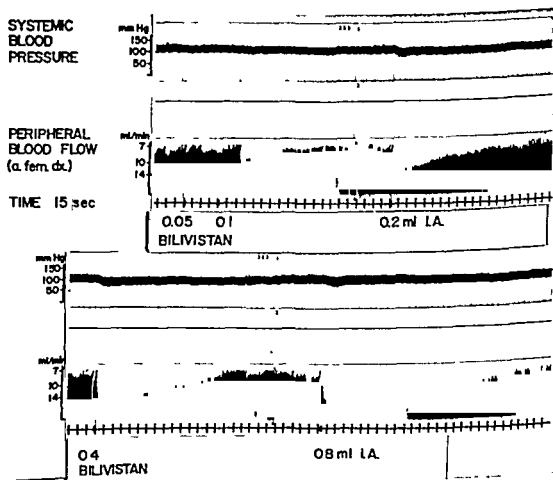


Fig 7 Vasodilatory effect of increasing doses of Bilivistan injected intra-arterially

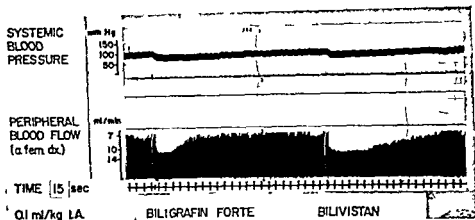


Fig 8 Comparison between vasodilatory effects of intra arterial injections (0.1 ml/kg) of Biligrafin forte and Bilivistan

dose response correlation. A characteristic experiment is illustrated in Fig 7. As has been observed with other parenterally administered contrast media, Bilivistan produced vasodilatation with increased flow in the femoral artery. As considerable differences in vascular reactive sensitivity may be observed from animal to animal of the same species it seemed to be of little interest to compare recordings of this kind with previously published data for Biligrafin forte (LINDGREN & SALTZMAN).

Instead, a series of experiments was performed in 9 cats that were given a dose of 0.1 ml/kg of Biligrafin forte. The increase in peripheral blood flow caused by the injection of Biligrafin forte is expressed in Fig 8. The flow increased from a flow of 1.5 (160 to 203) ml/min to 10 (160 to 203) ml/min. The circulatory increase lasted on an average for 2.3 minutes (1.5 to 4) after Biligrafin forte and for 3.5 minutes (2 to 5) after Bilivistan. Fig 8 is of a typical experiment.

*Histologic examination of the kidneys.* LINDGREN et coll (1966), in an earlier paper observed that the rapid intravenous injection of Biligrafin forte in a dose of 1 ml/kg bodyweight gives rise to histologically demonstrable renal changes in cats. Bilivistan in the same dose was injected rapidly through a catheter inserted in a brachial vein in three anaesthetized cats. The kidneys were removed 15 minutes later and subjected to histologic examination. Three other cats were anaesthetized in the same way and a catheter was placed in a brachial artery. No contrast medium was injected in these three control animals, but the kidneys

were removed after the same time had elapsed after the anesthetization and catheterization. The histologic appearances in the kidneys were similar in all these six cats, and no pathologic changes were demonstrated.

### Conclusions

Clinical experience with Bilivistan as a contrast medium for intravenous cholangiography indicated that this preparation has good diagnostic properties. When the right conditions are present, the contrast concentration obtained in the bile ducts is fully satisfactory.

The frequency of side effects is not particularly high. Severe reactions are rare, but cannot be entirely excluded. As with Biligradin forte a fall in blood pressure, which in isolated cases may lead to circulatory collapse, must be expected. Owing to the difficulty of obtaining wholly comparable materials, it has not been possible to make clinical comparisons between Biligradin and Bilivistan on a fully satisfactory scientific basis.

Irrespective of which contrast medium is used, the injection speed is obviously a decisive factor in the frequency and severity of the side effects. There is good reason to wonder whether infusion cholangiography (COOPERMAN et coll., and others) is not the best method for obviating the risk of side effects. This question has not been investigated in the present paper, however.

Cholangiography with Bilivistan as the contrast medium, must be regarded mainly as a method for examination of the biliary tract. In view of the frequency of side reactions and the layering phenomenon, intravenous cholangiography should in general not be used for examination of the gallbladder. In acute abdominal cases in which surgical intervention is being considered the use of cholangiography may however be justified as a time-saving measure for assessing filling of the gallbladder. Intravenous cholangiography is of course the only alternative in cases in which conditions causing obstruction to passage and resorption are present and prevent the use of oral cholecystography.

Experimental investigations on the circulatory effects in cats revealed that intravenous injections of clinical doses of Bilivistan caused a fall in blood pressure, but the fall was definitely smaller than that observed after Biligradin forte. It should be stressed however, that Bilivistan by no means lacks circulatory effects to a degree that could be considered clinically desirable, and the Bilivistan effect is much more marked than the effects recorded after intravenous administration of modern urographic and angiographic contrast media. After intra-arterial injection, which is not practised in clinical work, there occurred vascular dilatation with an accompanying increase in the blood flow of approximately the same magnitude as is observed after the use of Biligradin forte.

Although the increase in the blood flow was practically the same, the direct, vascular effect of Bilivistan could be said to be slightly more marked than for Biligrafin forte, as it lasted for a slightly longer time. In earlier comparisons between different contrast media, parallelism has always been noted between a fall in blood pressure after intravenous injection and vascular dilatation (increase in blood flow) after intra arterial injection. This did not appear to occur with Bilivistan and Biligrafin forte. The material is hardly large enough to permit definite conclusions, but the results possibly justify the assumption that the fall in blood pressure after intravenous injection of contrast medium may be due to other factors than reduced peripheral resistance. Among the possible factors, intravascular erythrocyte aggregation, impaired myocardial function, and an effect on autonomous centres in the central nervous system could be mentioned.

Intravenous injection of Bilivistan in cats did not produce any histologic renal changes of the type previously seen after similar doses of Biligrafin forte.

Thus the experimental investigations suggested that intravenously administered Bilivistan has lower toxicity than Biligrafin forte.

### Acknowledgements

The authors wish to express their appreciation to Prof. C. M. Fajers for the histologic examinations. The investigation was supported by Grant No. B 67 14 200701 from the Swedish Medical Research Council.

### SUMMARY

Ioglycamide (Bilivistan) has been tried as a contrast medium in 500 consecutive intravenous choleographies. The filling of the gallbladder was also evaluated and compared with the filling obtained after oral cholecystography in 179 of these patients. Experiments in cats were performed to ascertain whether Bilivistan causes circulatory effects or histologic renal changes. Bilivistan seemed an excellent contrast medium for examinations of the bile ducts after intravenous injection but did not appear to offer any advantages in examinations of the gallbladder.

### ZUSAMMENFASSUNG

An 500 aufeinanderfolgenden intravenösen Cholegraphien wurde Ioglycamid (Bilivistan) als Kontrastmittel ausprobiert. Die Füllung der Gallenblase wurde abgeschätzt und mit der Füllung die nach oraler Cholecystographie in 179 dieser Patienten erhalten wurde verglichen. An Katzen wurden Versuche angestellt, um Kreislaufstörungen und histologische Veränderungen, die dem Kontrastmittel zugeschrieben werden konnten, zu studieren. Bilivistan scheint ein ausgezeichnetes Kontrastmittel bei Untersuchungen der Gallenwege nach intravenöser Injektion zu sein, aber bei Untersuchungen der Gallenblase bietet es keine Vorteile.

were removed after the same time had elapsed after the anesthetization and catheterization. The histologic appearances in the kidneys were similar in all these six cats, and no pathologic changes were demonstrated.

### Conclusions

Clinical experience with Bilivistan as a contrast medium for intravenous cholegraphy indicated that this preparation has good diagnostic properties. When the right conditions are present, the contrast concentration obtained in the bile ducts is fully satisfactory.

The frequency of side effects is not particularly high. Severe reactions are rare, but cannot be entirely excluded. As with Biligrafin forte a fall in blood pressure, which in isolated cases may lead to circulatory collapse, must be expected. Owing to the difficulty of obtaining wholly comparable materials, it has not been possible to make clinical comparisons between Biligrafin and Bilivistan on a fully satisfactory scientific basis.

Irrespective of which contrast medium is used, the injection speed is obviously a decisive factor in the frequency and severity of the side effects. There is good reason to wonder whether infusion cholegraphy (COOPERMAN *et coll.*, and others) is not the best method for obviating the risk of side effects. This question has not been investigated in the present paper, however.

Cholegraphy with Bilivistan as the contrast medium, must be regarded mainly as a method for examination of the biliary tract. In view of the frequency of side reactions and the layering phenomenon, intravenous cholegraphy should in general not be used for examination of the gallbladder. In acute abdominal cases in which surgical intervention is being considered the use of cholegraphy may however be justified as a time-saving measure for assessing filling of the gallbladder. Intravenous cholegraphy is of course the only alternative in cases in which conditions causing obstruction to passage and resorption are present and prevent the use of oral cholecystography.

Experimental investigations on the circulatory effects in cats revealed that intravenous injections of clinical doses of Bilivistan caused a fall in blood pressure, but the fall was definitely smaller than that observed after Biligrafin forte. It should be stressed however, that Bilivistan by no means lacks circulatory effects to a degree that could be considered clinically desirable, and the Bilivistan effect is much more marked than the effects recorded after intravenous administration of modern urographic and angiographic contrast media. After intra-arterial injection, which is not practised in clinical work, there occurred vascular dilatation with an accompanying increase in the blood flow of approximately the same magnitude as is observed after the use of Biligrafin forte.





## RÉSUMÉ

Les auteurs ont essayé Diglycéramide (Bilivistan) comme moyen de contraste dans 500 cholangiographies intraveineuses consécutives. Ils ont aussi étudié l'opacification de la vésicule biliaire et la comparer avec l'opacification obtenue après cholecystographie par voie orale chez 179 de ces malades. Ils ont fait une expérimentation sur des chats pour déterminer si le Bilivistan a des effets circulatoires ou cause des lésions histologiques rénales. Le Bilivistan parait être un excellent moyen de contraste pour l'examen des voies biliaires après des injections intraveineuses mais ne parait pas présenter d'avantages pour l'examen de la vésicule biliaire.

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Table 1

*Age and sex distribution of the 42 patients in the series*

|       | 11-20 | 21-30 | 31-40 | 41-50 | 51-60 | 61-70 | 71-80 | Total |
|-------|-------|-------|-------|-------|-------|-------|-------|-------|
| Men   |       |       | 2     | 7     | 7     | 9     | 3     | 28    |
| Women | 3     | 4     |       |       | 2     | 3     | 2     | 14    |
| Total | 3     | 4     | 2     | 7     | 9     | 12    | 5     | 42    |

RIS & BROWN 1968, BERTELSEN 1969a, FLUTE et coll 1969, MAJOR & GALLOWAY 1969 MAJOR et coll 1969a, b and ROBERTSON et coll 1969)

From these premises the present writer has aimed to improve the technique of phlebography in cases with only indirect signs of thrombosis in order to facilitate the direct demonstration of floating thrombi and venous segments filled with non adherent thrombi

*Material* This was composed of 42 patients with clinical signs of acute deep venous thrombosis of the lower limb, or, in some, exacerbation of an older thrombosis. All were examined by ascending phlebography with a conventional technique as well as by a new method developed by the writer. Both examinations were performed on the same 47 occasions in 44 limbs. Three limbs were examined twice in two patients before and after treatment, and in the third patient the phlebographies were repeated on clinical signs of recurrent thrombosis of the same leg 9 months after the first thrombosis.

The patients included were those who from April 1968 to December 1969 were referred for phlebography on suggestion of acute venous thrombosis and in whom during conventional ascending phlebography direct or indirect signs of thrombosis were apparent. A few patients were excluded because examination by both methods could not be accomplished. No other selection of patients was made.

In 11 patients history of an earlier thrombosis situated elsewhere was recorded. In eleven patients conditions predisposing to thrombosis were present: recent major surgery (six patients), fracture or soft tissue injury of the lower limb (four patients), or infusion via the femoral vein during intensive care (one patient). Furthermore, in some twelve patients, other factors such as heart disease, dehydration, bed rest during infectious or systemic disease, a lengthy period of sitting late pregnancy, or withdrawal of dicumarol administration may have influenced the development of thrombosis. Five women were on peroral contraception at the start of the disease.

## PHLEBOGRAPHY IN ACUTE DEEP VENOUS THROMBOSIS OF THE LOWER EXTREMITY

A comparison between centripetal ascending and  
descending phlebography

by

ULF BERGQVIST



The inherent inaccuracy in the clinical diagnosis of deep venous thrombosis is well established, while the results of phlebography are generally considered reliable (COON & COLLIER 1959, McLACHLIN et coll 1962, BORGSTROM et coll 1965, HÄGER 1969, BRODEIUS et coll 1970, among others)

Directly demonstrated intravascular thrombus leaves no doubt about the diagnostic accuracy of phlebography. The duration of symptoms and signs varies considerably, and often only indirect signs of thrombosis are obtained at phlebography. Small or large regions of the deep venous system may fail to fill with contrast medium, and secondary flow changes may also occur. Several sources of error must then be considered (ALMÉN & NYLANDER 1964, HJELMSTEDT & BERGVALI 1968, ZACHRISSON 1969), and the accuracy of diagnosis is diminished. Furthermore the presence of residues of an earlier thrombosis may render the evaluation of recent changes difficult.

The demands upon the information obtained by phlebography have become greater as a result of increasing interest in surgical and active thrombolytic therapy of thrombosis (FOGARTY et coll 1966, HALIER 1967, BROWSE et coll 1968, HAR-

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Table 2

A total of 47 examinations classified from findings at centripetal ascending phlebography in the semi erect position (CAP) as well as according to the proximal extension of the thrombosis — Below the horizontal double line are the corresponding numbers of examinations with additional findings at supplementary centripetal descending phlebography in the form of floating or non adherent thrombi (CDP)

| CAP findings                     |           | Direct signs in 24 examinations |    |   | Indirect signs in 23 examinations |    |    | Total 47 |
|----------------------------------|-----------|---------------------------------|----|---|-----------------------------------|----|----|----------|
| Proximal extension of thrombosis | Lower leg | 8                               |    |   | 1                                 |    |    | 9        |
|                                  | Thigh     |                                 | 10 |   |                                   | 10 |    | 20       |
|                                  | Pelvis    |                                 |    | 6 |                                   |    | 12 | 18       |
| <hr/>                            |           |                                 |    |   |                                   |    |    |          |
| CDP additional direct findings   | < 5 cm    | Lower leg                       | 4  | 2 | 1                                 | 1  | 3  | 11 (*)   |
|                                  |           | Thigh                           |    | 1 |                                   | 1  | 2  | 4        |
|                                  | > 10 cm   | Lower leg                       |    | 1 |                                   | 2  | 2  | 5        |
|                                  |           | Thigh                           |    |   |                                   | 2  | 4  | 6        |
|                                  | Total     |                                 | 4  | 1 | 3                                 | 1  | 6  | 11       |

\* Main findings in the thigh separate findings also in the lower leg  
Groups within dotted line displayed separately in Table 3

60° A further 40 to 60 ml of the contrast medium was injected through the same cannula as at centripetal ascending phlebography. Films were obtained of the lower leg and thigh in two projections at right angles, one invariably with a horizontal beam direction. Sometimes, films were also obtained of the upper thigh and pelvic regions in the a.p. projection while the leg was still elevated. This technique is defined as centripetal descending phlebography. Venous stasis was applied below the groin, except in about a quarter of the patients in whom the venous return of the leg was already considerably reduced by the thrombosis. The duration of the induced stasis was usually less than 60 seconds.

A further examination of the iliac veins was performed in 21 patients, with injection of contrast medium either after direct puncture of the femoral vein in the fossa ovalis or by catheterisation from the other side. The iliac vein examinations were carried out to assess the proximal level of thrombosis prior to a contemplated thrombectomy.

A directly demonstrated thrombus was defined as a defect in a contrast filled vein, distinctly outlined, situated at the same level and seen in at least two different projections. These criteria were fulfilled by all remembered

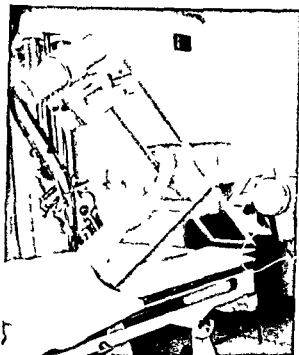


Fig 1 Arrangement for centripetal descending phlebography

It was always attempted to make an accurate estimate of the duration of clinical symptoms and signs prior to the phlebographic examination

Surgical thrombectomy was performed in ten patients, in one of these the new technique of phlebography was used only after the operation Eight patients were treated by active thrombolysis with streptokinase, two of them after thrombectomy An analysis of the results of therapy has not been considered to fall within the scope of the present report

*Methods* Centripetal ascending phlebography was carried out in all the patients according to the technique of GREITZ (1954) The patient stood leaning against the examination couch at an angle of  $60^{\circ}$  to  $65^{\circ}$  to the horizontal plane, and 60 to 80 ml Urografin 45 % were injected into a superficial vein of the foot Films were obtained of the lower leg, the knee and the lower and middle thigh regions in at least two different projections The upper thigh and pelvic regions were examined in the a p projection only

Thrombosis, directly or indirectly demonstrated, was an indication for a supplementary examination, which was performed as follows The leg was placed, with the foot elevated, in a simple support on the horizontal examination couch (Fig 1) The inclination to the horizontal plane was usually  $30^{\circ}$ , but sometimes



Fig. 2 Long segment of popliteal femoral veins unfilled at centripetal ascending phlebography (a) but patent at centripetal descending phlebography (b)

Fig. 3 At centripetal ascending phlebography the contrast medium in the popliteal vein gradually disappears proximally (a) while the lower pole of a floating thrombus ( $\rightarrow$ ) is seen in the femoral vein at centripetal descending phlebography (b)

## Results

Two of the forty two patients had bilateral lower limb thromboses and one had two separate episodes of thrombosis in the same leg. Thus, out of 45 instances, the left leg was involved in 25 instances and the right one in 20, or a ratio  $L/R \approx 25/20 \approx 1.25$ . Of the ten patients in whom the thrombosis reached to the common iliac vein it was on the left side in eight patients, which gives the ratio  $L/R \approx 8/2 \approx 4.00$ . Six thromboses were directly demonstrated as reaching up to the inferior vena cava, all on the left side. In nine patients, the thrombosis was confined to the lower leg veins, five on the left and four on the right side. The thrombosis was never confined to the iliac veins.

Thrombi were directly demonstrated by centripetal ascending phlebography in

Table 3

*Additional directly demonstrated thrombi at the supplementary centripetal descending phlebography (CDP performed in the twenty two patients in whom the examination of thrombosis extending above the knee is difficult by means of centripetal ascending phlebography in the semi erect position had given only indirect signs*

| Proximal extension of thrombosis   |        | Thigh     | Pelvis | Total | Percentages of the twenty two examinations in the different groups |      |
|--|--------|-----------|--------|-------|--|------|
| CDP additional direct findings differentiated as regards length and site | ~ 5 cm | Lower leg | 1      | 3     | 4  | 32 % |
|  |        | Thigh     | 1      | 2     | 3  |      |
|  | 10 cm  | Lower leg | 2      | 2     | 4  | 45 % |
|  |        | Thigh     | 2      | 4     | 6  |      |
|  | Total  |           | 6      | 11    | 17   | 77   |

that were largely non-adherent to the wall of the vein, as demonstrated at centripetal descending phlebography. A positive diagnosis in these instances required the presence of contrast medium between the wall of the vein and the thrombus on both sides in one projection, but only on one side in the other, the latter usually being the lateral projection with a horizontal beam direction. At descending phlebography in this projection the heavy contrast medium was often seen to gather along the lower part of the vein around the inferior surface of the thrombus. At the same time no medium, or only a thin layer, was sometimes observed between the superior surface of the thrombus and the wall of the vein. The findings in the a.p. projection were then decisive for reaching a positive diagnosis. When contrast medium was seen on both sides of the thrombus in one projection and on a further side in the other projection it was considered reasonable to assume that the thrombus was largely non-adherent to the wall of the vein. To require that the contrast medium be demonstrated on both sides of the thrombus in both projections in such instances would have led to an obvious underrating of non-adherent thrombi.

A mural thrombus adherent to the wall of the vein on one side and only partly filling the lumen may be difficult to classify. However, such mural thrombi were seen only rarely in this series of patients, and never as an isolated or dominant finding. Mural thrombi were therefore not registered. Nor were thrombi in superficial veins taken into account.



Fig 2 Long segment of popliteal femoral veins unfilled at centripetal ascending phlebography (a) but patent at centripetal descending phlebography (b)

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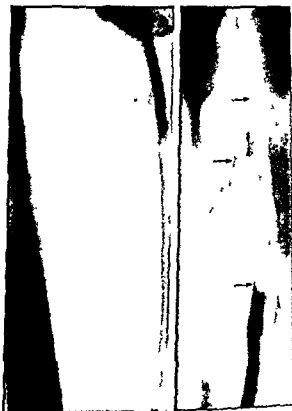


Fig 4 The deep veins could not be demonstrated with centripetal ascending phlebography (left view), but segments of the femoral veins filled with largely non-adherent thrombi ( $\rightarrow$ ), were revealed at centripetal descending phlebography (right view)

the deep venous trunks, muscle or perforator veins in 24 examinations, while only indirect signs of thrombosis were obtained in 23 instances. Additional information gained by centripetal descending phlebography in the form of floating or non-adherent thrombi is given in Table 2, separately for the two groups of centripetal ascending phlebography findings. The findings at descending phlebography are differentiated according to their extension and location as well as according to the extent of the thromboses. Only changes not demonstrated at ascending phlebography have been registered, and findings above the femoral vein have not been included, since the examination of the iliac veins was not carried out systematically.

In the group of 23 examinations with only indirect ascending phlebography findings, floating thrombi were demonstrated in the iliac veins in three instances. The upper pole of the thrombosis in another four patients was bulging more or less into the confluence of the inferior vena cava.

It will be seen from Table 2 that additional information was provided by descending phlebography in 26 instances, in the 47 examinations performed.

The additional descending phlebography findings in the twenty-two patients with thrombosis above knee level, in whom ascending phlebography had given

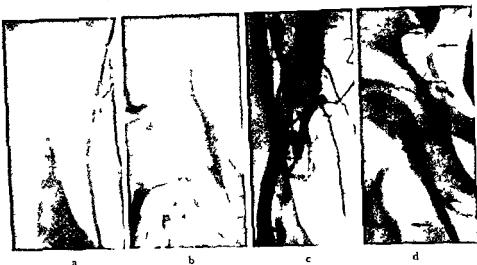


Fig 5 Lower and upper poles ( $\rightarrow$ ) of a long iliofemoral thrombus not demonstrable at centripetal ascending phlebography (a) and (b) but outlined by contrast medium at centripetal descending phlebography (c) and (d)

only indirect signs, are tabulated separately in Table 3. This group of femoral or iliofemoral thromboses is important from a clinical point of view. As appears from Table 3, additional information by descending phlebography was in this group gained in a total of 17 patients out of 22 (77%), concerning relatively long venous segments in 10 out of 22 patients (45%).

The findings in one patient with a thrombosis reaching up to the inferior vena cava will be described in some detail. Ascending phlebography yielded only indirect signs of thrombosis. At descending phlebography a short thrombosed segment was directly demonstrated in the lower leg and the case was accordingly referred to the group 'additional CDP findings  $< 5$  cm' in the tables. However, a more than 20 cm long segment of the popliteal femoral vein, unfilled by contrast medium at ascending phlebography, was also found to be patent at descending phlebography (Fig 2). This finding cannot be registered according to the criteria but must rightly be referred to the group of iliofemoral thromboses in which additional information of long venous segments was obtained at descending phlebography. Thus in the clinically important category of thromboses above knee level, descending phlebography gave substantial additional information concerning long venous segments in eleven patients out of twenty two, or 50%.

The findings at descending phlebography, which in Tables 2 and 3 were classified  $> 10$  cm, in the majority of the patients corresponded to floating or



Fig 4 The deep veins could not be demonstrated with centripetal ascending phlebography (left view), but segments of the femoral veins filled with largely non adherent thrombi ( $\rightarrow$ ), were revealed at centripetal descending phlebography (right view)

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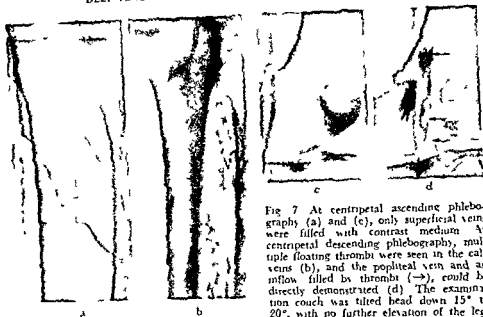


Fig 7 At centripetal ascending phlebography (a) and (c), only superficial veins were filled with contrast medium. At centripetal descending phlebography, multiple floating thrombi were seen in the calf veins (b), and the popliteal vein and an inflow filled by thrombi ( $\rightarrow$ ), could be directly demonstrated (d). The examination couch was tilted head down  $15^\circ$  to  $20^\circ$ , with no further elevation of the leg. No stasis was applied.

complained of an increase in local symptoms after phlebography but no signs of progress of the thrombosis attributable to the investigation were registered.

### Discussion

*Technique* A method of phlebography similar to centripetal descending phlebography was described by MARK (1943) for use mainly in cases of varicose veins and swollen legs. Although this was claimed to secure a better representation of the deep veins than the conventional technique of that time with the patient in horizontal position, MARK apparently did not develop the method further.

The basis of development for the technique of centripetal descending phlebography was the results of the clinical and experimental studies of the distribution of contrast media in veins in different positions, published by GRETTZ. These results indicated that veins to be examined should be positioned in the vertical plane, or near to it, to avoid layering of blood and contrast medium which might make an evaluation impossible. The leg should therefore be elevated at least  $60^\circ$  from the horizontal plane at descending phlebography. However, few patients with symptoms of an acute thrombosis of a deep leg vein are able to elevate the leg to such a degree, on account of pain, but most of the patients can manage

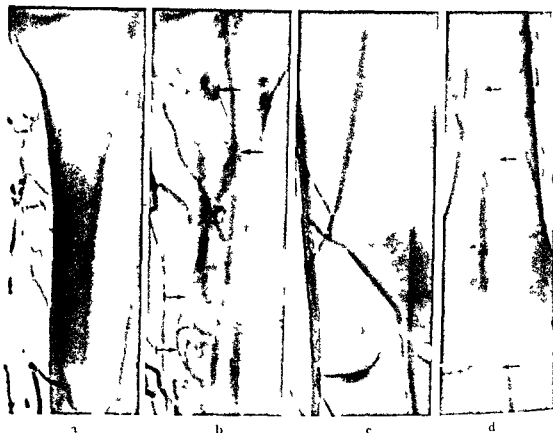


Fig 6 In the lower leg (a) and (b) and in the thigh (c) and (d) the short thrombus filled deep venous segments (→) not seen at centripetal ascending phlebography could be directly demonstrated by centripetal descending phlebography (b) and (d). There is also a floating thrombus (→) in a muscle vein in the calf (b).

non adherent thrombi, 10 to 15 cm in length (Figs 3 and 4). In a few cases 20 to 30 cm long thrombus-filled venous segments were seen (Fig 5). Small (<5 cm) additional centripetal descending phlebography findings are illustrated in Fig 6.

Slight or moderate clinical signs of pulmonary embolism were observed in three patients 5 weeks to 3 days before phlebography. In one of these patients, the clinical diagnosis was verified by pulmonary scintigraphy and angiography. After thrombectomy followed by streptokinase therapy a fourth patient died from acute arterial haemorrhage, a month after ascending and descending phlebographies and 2 and 3 weeks after further examinations with ascending phlebography. No clinical signs of pulmonary embolism were noted in this patient but a small pulmonary embolus was present at autopsy. This finding cannot be related to the phlebographies and cannot be assumed to have influenced the outcome.

No complications were noted during or after phlebography. A few patients



Fig 9 At centripetal ascending phlebography (left view), only the superficial veins were seen. At centripetal descending phlebography with an elevation of  $60^{\circ}$  (right view), thrombus filled deep venous trunks of the lower leg could be demonstrated (they were also seen at an elevation of  $30^{\circ}$  but not so extensively). No stasis was applied.

of contrast medium so that a high pressure level should be avoided. According to experience, 70 mm Hg in an ordinary blood pressure cuff should as a rule be sufficient and is usually well tolerated.

The occurrence of venous segments devoid of contrast medium is characteristic at descending phlebography with stasis, due to blood being held behind effective valves so that a sharp interphase appears at the valves (Fig 8). This phenomenon is recognized without difficulty and, according to the present author's experience, confusion with thrombosis is unlikely.

Since short or long venous segments are often unfilled by contrast medium during descending phlebography, the technique is intended as and only suitable as a supplementary measure for the evaluation of the anatomy in areas not accessible with ascending phlebography due to flow conditions.

The heavy contrast medium at ascending phlebography mainly follows the blood stream, though the force of gravity works in the opposite direction. When occlusion of a deep vein is present, the blood-contrast medium mixture passes round it through collateral vessels. The by-passed venous segment may include not only the occlusion but also a peripheral segment where in spite of patency no obvious flow occurs. The length of the by-passed segment varies with the situation.



Fig 8 Characteristic appearance of interphase by effective valves ( $\rightarrow$ ) at centripetal descending phlebography with stasis

a 30° elevation without too great discomfort. Initially, a few examinations were carried out with tilting of the whole examination couch, head down about 20°, with satisfactory diagnostic results (Fig 7). Furthermore, no obvious difference from a diagnostic viewpoint between the results obtained with 30° and 60° elevations was found in a limited number of patients. Since the positive findings at descending phlebography with an elevation of 30° were consistent, and layer formation could be assessed through the horizontal beam projections, 30° elevation was considered to be a suitable compromise.

GRFITZ has pointed out that layer formation between blood and contrast medium is most marked in extremities examined in the vertical position when the flow of blood is directed downwards. Descending phlebography in the present group of patients was performed with the venous return severely impeded either by the thrombosis or by the use of central venous stasis through an inflated cuff around the proximal part of the thigh. Stasis was employed in patients without impediment of the venous return, as estimated at ascending phlebography. With no blocking of the return, a marked layering of contrast medium occurs during descending phlebography and the medium rapidly disappears from the elevated limb without affording any diagnostic information.

Stasis should imply, as far as possible, a complete blocking of the venous return. A high pressure level often causes severe pain in acute thrombosis, similar to the Lowenberg sphygmomanometer cuff pain test used in clinical diagnosis (CECIL & LOEB 1967). The pain is accentuated by the administration

the upper part of the thigh and 40 ml of contrast medium are injected into the

no stasis was used and the contrast medium was injected in the foot for lower leg phlebography as well as in the groin for retrograde phlebography of the femoral vein (as described by GULLMO 1957). No comparison of the different techniques was presented. The reason for modifying the technique was not stated but may have been the risk of bleeding from the femoral vein puncture in patients treated by thrombolytic agents.

*The reliability of the methods* Applying the afore mentioned criteria, which are essentially the same as those proposed by BORGSTROM et coll and used by BECKER et coll (1970), the diagnostic accuracy should be the same with centripetal descending phlebography as with centripetal ascending phlebography. The latter is considered to be very reliable by BECKER et coll. Disturbing flow effects are to some extent reduced at descending phlebography and this may facilitate evaluation of positive findings. Diagnosis by descending phlebography is not difficult in practice.

*Haemodynamic aspects* HÆGER & NYLANDER (1967), NYLANDER (1968) and BRODELIUS et coll (1969) described a finding stated to be characteristic of acute lower leg thrombosis, which consisted of exclusive contrast filling of the superficial veins of the lower leg and secondary changes of flow 'the derivated flow phenomenon' and 'the knot hole phenomenon'. The latter was said to be the result of increased pressure under the crural fascia caused by the thrombus.

... on ascending thrombi was dominant. The differences were considered to reflect divergent principles in selecting the patient series.

In the present series, exclusive contrast filling of superficial veins was

... by NYLANDER and coworkers have not been observed. In eight of the cases deep crural thrombi were directly demonstrated at descending phlebography. Two such instances, in which thrombi were seen at elevations of 20° and 30° to 60° without stasis are presented in Figs 7 and 9. These two patients had thrombosis reaching up to the inferior vena cava. The examples suggest that a high subfascial pressure in the calf may not be the only or the most important factor at work when the deep crural veins fail to fill at conventional phlebography.



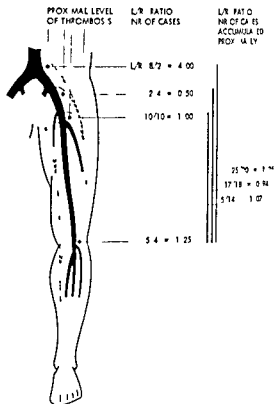


Fig. 10 Left/right distribution of 15 thromboses. Ratios varying with the proximal extension level of thrombosis and consecutively accumulated ratio figures from lower leg in proximal direction.

and the capacity of the collaterals. Shorter or longer venous segments may thus fail to fill. An accurate demonstration of the true extent of the block can be obtained only by directing the contrast medium to the by-passed but patent venous segment. This may be accomplished at descending phlebography by the help of the force of gravity provided the blood flow is impaired to a sufficiently high degree.

GUILMO (1956) has described a technique of phlebography in which the contrast medium was injected into the popliteal vein after direct puncture. This should offer better prospects for demonstration of the femoral vein than injection into a vein of the foot in thrombosis. GUILMO reported failure to obtain direct puncture of the popliteal vein in about one out of six cases, however, and this may be even more difficult in acute venous thrombosis. A further important argument against this technique is that puncture of deeply situated veins should be avoided, as far as possible, when thrombolytic treatment may be instituted, due to the risk of bleeding from the puncture site (ROBERTSON 1969).

BRODELIUS, LORING & NYLANDER (1969) report a modified technique of phlebography for the examination of acute venous thrombosis. The patient is placed in the supine horizontal position, a tourniquet is applied tightly around

hours old will rarely become detached" "After an interval of several days and after development of a secondary inflammatory reaction in the wall of the thrombosed vein, there may be a sudden proximal extension from the end of the old organizing thrombus"

The reactions between the thrombus and the wall of the vein have been investigated experimentally by BERTELSEN (1969b), who observed a close time relationship between the mural damage to the vein, the adhesion of the red thrombus to the venous wall and the tendency to rethrombosis following thrombectomy IKWIGER (1963), from a clinical material of thromboses and emboli studied by histologic methods, described six separate stages during the process of organization and recanalisation There is, however, a considerable time overlap between the earlier stages, as has also been reported by LEU (1968)

The degree of local clinical signs caused by the thrombosis, pain and swelling, is dependent upon the degree of involvement of the venous wall as well as upon the capacity of the collateral vessels available MAYOR & GALLOWAY (1967) have indicated that the collateral drainage is decisive for the extent of the signs in iliofemoral thrombosis, and that the prospects of venous drainage decrease the more proximal the thrombosis is situated Small thrombi often run a silent course (BORGSTROM et coll, HAAKAR et coll 1969, BECKER et coll) Even extensive thrombosis may give surprisingly few symptoms or signs This has been stressed by BRODELLIS et coll (1970), who reported a considerable discrepancy between clinical signs and phlebographic findings in a large number of patients in a series of 275 thromboses This was not as frequent in the present material since all patients were referred for phlebography on the clinical suggestion of thrombosis with usually obvious signs

Like the clinical signs, the duration may also be misleading According to MAYOR & GALLOWAY (1969), iliofemoral venous thrombosis is often a slow insidious process, and a stage of partial or incomplete occlusion of the vein may be present for weeks or months and detectable only by phlebography They noted that even when iliofemoral occlusion is of recent clinical origin, an old adherent thrombus may be present and to some extent compromise complete clearance

The duration of symptoms or signs in the present series of patients varied over a wide range, i.e. from 0 to 12 hours up to about 10 weeks The history was often vague and difficult to evaluate The period of symptoms or signs prior to phlebography was on the average shorter in the group with direct ascending phlebography findings, though even among these cases a duration of 5 to 7 weeks was noted in some instances In the group with only indirect findings at ascending phlebography, no particular difference was found in this respect between the cases with direct descending phlebography findings of thrombosis and the remainder The age of a thrombus can only in an experiment be known with

It should also be mentioned in this context that in some ten patients floating thrombi in muscle and perforating veins of the lower leg were demonstrated at descending phlebography in veins unfilled at ascending phlebography.

The left/right distribution of thrombosis in this series approaches a ratio L/R of 5/4, which is relatively low compared with other reports. The overall left side dominance is dependent mainly on the group of thromboses reaching the common iliac vein with a ratio L/R of 8/2 (Fig. 10). In one instance only can the iliac veins be stated definitely to have been the site of the primary thrombus, as indicated by phlebography before thrombectomy. It seems reasonable to assume that among the thromboses found in the iliac veins further cases exist in which the site of the primary thrombus was also iliac. The history of the patient and the phlebographic findings more or less confirm this assumption in some ten further patients. The findings indirectly imply that the causative factor of the left side dominance is operative mainly when the origin is proximal, while the influence on thromboses commencing at the periphery is much less or absent. A contributory mechanism may be that the tendency to proximal propagation of peripheral thromboses is more marked on the left side.

According to MAYOR & GALLOWAY (1969), thrombosis involving the whole length of the iliofemoral segment commences in this segment and from their findings at thrombectomy it appears that a high onset of thrombosis with distal propagation is by far more frequent than a low onset with proximal propagation. They also call attention to the fact that iliofemoral thrombosis may occur simultaneously to a more peripheral deep vein thrombosis rather than as a result of propagation from the periphery.

The cause of the bias towards the left side in thrombosis is considered to be a proximal flow impediment in the left common iliac vein. Regarding its nature different opinions are encountered in the literature (MAY & NISSE 1959; GULLMO 1964; COCKET *et coll.* 1967; MAYOR & GALLOWAY 1969; NEGUS *et coll.* 1969).

*Clinical aspects.* The first phase of all thrombus formation is platelet adhesion and aggregation (NILSSON 1967). A venous thrombosis is made up of a relatively small platelet plug, the white head, and a larger coagulation thrombus forming the red body and tail. In the work by ALLEN *et coll.* (1966) the evolution of thrombosis is described as follows: The red or lamellated tail of the thrombus may float free in the blood stream for a short time but soon tends to adhere to the endothelium and when this adherence occurs organization by fibroblasts from the endothelium follows rapidly and completes the adhesion. As the propagating body and tail of any thrombus extend, a portion or all may detach and become an embolus. It is almost certain that a thrombus that is more than three days old will not become detached and a thrombus that is more than a few

## ZUSAMMENFASSUNG

Es wird über die Befunde in 42 Patienten mit Thrombose der unteren Extremität, die mittels centripetaler aufsteigender Phlebographie sowie mittels einer neuen Methode, die centripetale absteigende Phlebographie genannt wird, berichtet. Mit konventioneller Phlebographie konnten in der halben Anzahl der Patienten nur indirekte Zeichen einer Thrombose, während mit der neuen Methode in drei Viertel dieser Patienten flottierende Thrombosen, demonstriert werden konnten.

## RÉSUMÉ

L'auteur décrit sur une série de 42 malades, atteints de thrombose aiguë des veines profondes des membres inférieurs les résultats de la phlebographie ascendante centripète et d'une nouvelle technique, la phlebographie descendante centripète.

mobiles

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certainly. For practical reasons the time factor is important since thrombectomy as well as thrombolytic therapy yield far better results in the earlier stages of thrombosis (HAFFER, BERTELSSEN; ROBERTSON)

In the individual patient, an acute venous thrombosis may often, except when small, be considered to consist of several parts of different ages impossible to determine. An indirect estimation of age, as implied by the demonstration of floating or non-adherent thrombi at phlebography, will in practice be as useful. It is furthermore the only way to find out with reasonable accuracy whether at least that part of a thrombosis where such findings are made is fresh and accessible to active therapy.

The importance of performing phlebography in such a way that floating or non-adherent thrombi may be demonstrated is obvious. The additional information obtained at descending phlebography should be judged against this background. In the present series, relevant clinical information on the extension of the thrombosis and its relation to the venous wall has been gained about long venous segments in nearly half the number of patients, which in this respect could not be evaluated at ascending phlebography. The thrombosis was always situated in the femoral and iliac veins, and thus belonged to the most important clinical group as regards the risk of embolism as well as damage to venous function.

In the ten patients with thrombectomy, the findings at phlebography were verified at operation.

### Conclusions

A clinical suggestion of acute deep vein thrombosis should be confirmed by ascending phlebography. Equivocal findings or only indirect signs of thrombosis should constitute indications for a supplementary examination by centripetal descending phlebography according to the new technique described. It may also be necessary to carry out an examination of the iliac veins to define the proximal extension of the thrombosis. Only by complete phlebographic investigation in this manner is a full evaluation possible, and this may be a decisive factor in the management of the patient. The new technique is simple to perform and no drawbacks have been encountered.

### SUMMARY

The results in a series of 42 patients with thrombosis of the lower limb examined by centripetal ascending phlebography as well as by a new technique called centripetal descending phlebography, are presented. Only indirect signs of thrombosis were obtained in half the number of patients by conventional phlebography but in three quarters of these non adherent thrombi were demonstrated with the new technique.

## ANGIOGRAPHY IN RENAL TUBERCULOSIS

by

R BJØRN HANSEN and T AARHUS

Tuberculosis of the kidney is no longer common. It may however still occasionally be encountered and the radiologist will play an important role in establishing the correct diagnosis and the extent of the lesion.

WEYDE (1952) reviewed 210 translumbar aortographies, 60 of which were performed in patients suffering from renal tuberculosis. He stated that the essential finding was decreased vascularity in the affected parts of the kidney. The vessels were atrophic, often irregularly outlined, varied in caliber and often presented abrupt terminations, they were sometimes stretched and displaced around the focus. The nephrograms contained more or less circumscribed areas of reduced accumulation of contrast medium. Similar findings were also reported by BALMANN & BAUNDISCH 1964, FRITJOFSSON & EDSSMAN 1959, ROHL *et coll* 1968 *inter alia*. The importance of selective angiography and angiotomography for a detailed mapping of parenchymal lesions was stressed by FRIMANN DAHL (1958, 1966).

There appears to be little in the literature on the findings in selective nephroangiography in tuberculosis of the kidneys. The purpose of the present investigation was therefore to study the nature and frequency of the pathologic changes. It was also decided to evaluate the yield of angiography compared with the information obtained by urography.

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Fig 2 Selective nephroangiography a) Arterial phase. Circumscribed avascular area in middle of kidney (arrow) b) Nephrographic phase. Shrinkage and absence of accumulation of contrast medium in the infarction

patients were subjected to urography at approximately the same time and the two investigations were compared

### Results

The *angiographic findings* in the forty three patients with renal tuberculosis were as follows

A decreased vascularity in the affected areas was the most frequent finding. The arteries had few branches which gave them a naked appearance that was characteristic in thirty two patients (74 %) (Figs 2, 4 and 5)

Irregular contours and caliber variation of the arteries were also frequent





FIG. 1 a Urograph. Irregular cavity in the middle calyx group (arrow) hydronephrotic appearances produced by abdominal compression b Selective nephroangiography of the same patient arterial and early nephrographic phases. Slightly polycyclic contours of the kidney possibly due to shrinkage but more likely to congenital lobulation

**Material and Method** The selective nephroangiograms of a total of forty-eight patients, examined during the period 1959—1967, were reviewed. Two patients with uncertain diagnoses and three examinations of inferior quality were excluded.

The material consists of the remaining forty-three patients with confirmed renal tuberculosis and satisfactory angiograms. The disease involved both kidneys in eight of the patients, two of these had had one kidney removed before our examination. The age varied from 28 to 67 years, average 44 years. Twenty-one of the patients were males, twenty two were females.

Abdominal aortography was performed via the femoral route and followed by bilateral selective nephroangiography in the supine and oblique positions. All

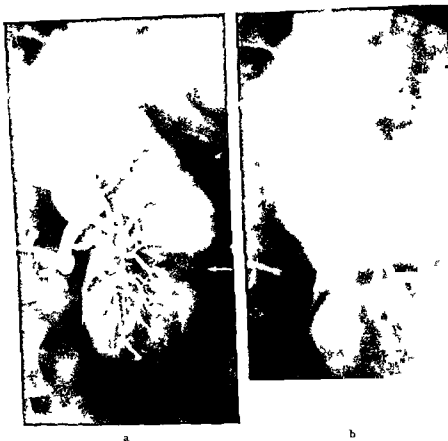


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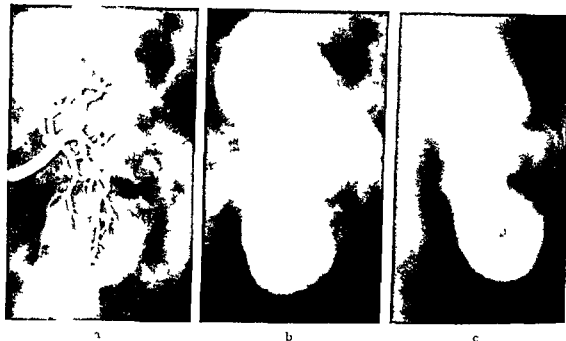


Fig 3 Selective nephroangiography. a) Arterial phase. Expansive vascular lesion with irregular calcifications in middle of kidney. b) Nephrographic phase. Improved demonstration of the lesion. c) Angiotomography. Further improvement in the demonstration of the parenchymal lesion.

findings. These were particularly common in the subsegmental or smaller arteries, and occurred in twenty patients (47 %) (Fig 5).

Occlusions or abrupt terminations, mainly in the subsegmental arteries, were present in eleven instances (25 %) (Fig 5).

Ten of the patients had signs of an expansive process within the kidney (Figs 3 and 5), the vessels being displaced and stretched around the lesions. Crowding of the arteries was noted in the tissue adjacent to the expansion in seven of these patients (Fig 5). Crowding of the arteries was also present in three patients with localized shrinkage of the kidneys.

An irregular, tortuous course of the arteries, reported to be common in renal tuberculosis, was seen in only five patients, and in all of these the changes were only moderate.

Retarded flow through the arteries of the affected area was demonstrated in three patients, the kidneys were much affected, with considerable atrophy of the arteries (Figs 4 and 5).

Prominent capsular or pelvic arteries, held to occur in inflammatory diseases of the kidney, were observed in eight patients (Fig 4).

Deformity of the kidneys was usually clearly demonstrated in the parenchymal



Fig 4 a) Urography Pelvic constriction with occlusion of the middle and upper calyces  
b) Selective nephroangiography nephrographic phase Delayed arterial emptying in upper half of kidney with few arterial branches (naked appearance), prominent capsular artery (arrow)

phase and occurred in twenty-eight patients (60%) (Figs 2, 3, 5 and 6). Circumscribed parenchymal defects were present in twenty-two patients (50%) (Figs 2, 3, 4 and 5). In several of these, the appearance of the defect suggested infarction (Fig 2).

The angiographic examination was considered to be normal in seven (16%) of the forty-three patients (Fig 1).

The urographic examination revealed pathologic changes in all patients.

Areas of destruction in the collecting system were the most common finding and were seen in thirty-six patients (84%) (Figs 1 and 7). The cavities varied in size from 0.5 to 2.5 cm.

Deformity of the collecting system was also a common feature. This included



Fig. 5. Selective nephroangiography in non functioning kidney. a) Arterial phase. Several expansive lesions in kidney with adjacent arteries displaced and crowded, irregular arterial caliber and abrupt terminations (arrows). b) Nephrographic phase. Delayed arterial emptying in lower pole, improved demonstration of affected avascular areas.

both strictures and occluded calices and occurred in thirty-three of the patients (77 %) (Figs 4 and 7).

A varying degree of hydronephrosis was present in nine patients, none of whom had enlarged kidneys, an observation similar to what was reported by DAUTREBANDE *et coll.* (1967). An additional eight patients had localized dilatation of the calyces.

Six patients had reduced function of the affected kidney as judged from urography. Three of these patients had decreased function only in the affected part of the kidney, while the remaining tissue seemed to possess normal function.

In two patients with extensive renal tuberculosis there was no observable excretion of contrast medium from the diseased kidney.

Renal deformities referable to expansion or shrinkage within the kidney were



Fig 6 Selective nephroangiography a) Nephrographic phase oblique projection Marked shrinkage with irregular contours of lower pole b) A.p. projection No definite renal deformity

demonstrated by urography in thirteen patients (30 %) Calcifications in the kidneys were noted in nineteen patients (44 %) (Fig 3) Pathologic changes in both kidneys were demonstrated in eight patients

### Discussion

Decreased vascularity resulted in appearances resembling infarction in several of the patients However, it was often difficult to decide whether this was referable to vascular occlusion or to primary parenchymal necrosis The possibility of vascular occlusion caused by infiltration or shrinkage in the adjacent tissue cannot be eliminated (AMBROSETTI & SESENA 1955) This seems to be a reasonable explanation of the irregular caliber of the arteries frequently noted in the present series

The stretching and crowding of the arteries around expansive tuberculous lesions had no specific features and could not be differentiated from the vascular displacement around lesions of other natures, e.g. cysts or non specific abscess formation



Fig 7 Urography. Marked pelvic constriction and large, irregular area of destruction in the lower pole

Increased vascularity in or around the tuberculous lesion was never obvious except for the crowding of arteries referable to parenchymal shrinkage or expansive lesions. The crowding of the arteries was usually not a prominent feature, perhaps because of simultaneously decreased vascularity. An increase in the number of capsular or pelvic arteries, probably referable to inflammatory changes in the capsule or renal pelvis, was not a frequent finding in the present material.

The spread of the disease and the presence of cortical deformity as well as intrarenal lesions were usually more clearly shown in the nephrographic phase. This has previously been stressed by OLSSON (1962), who stated that the nephrographic phase was more important than the arteriographic phase in the evaluation of the condition. The cortical defect could sometimes be demonstrated only in the oblique projection in the present series (Fig 6). The importance of obtaining films in two projections should therefore be stressed. Angiotomography may provide additional information by improved demonstration of the renal parenchyma (Fig 3c).

Changes in the renal collecting system were far better outlined in the urograms. Minor destruction of the papillae, which produced no angiographic changes, was usually evident at urography. Deformity of the collecting system, apparent as calyceal or pelvic strictures and secondary dilatation, well shown by urography, usually caused no angiographic changes. It should also be noted that

in this investigation the urographic examinations revealed pathologic changes in all the patients. Furthermore these changes were usually of a specific character and often suggested the tuberculous nature of the lesion. Urography is, however, of limited value in parenchymal lesions not connected with the calyceal system. In the present series the extension of the tuberculous lesion was often better demonstrated at the angiographic examination than by the urography. However, the angiographic findings were not diagnostic of tuberculosis, and the angiograms were considered normal in seven of the present patients, despite definite urographic evidence of tuberculosis.

The demonstration of the renal vascularisation affords an important aid in the selection of therapeutic means. A prerequisite for a good result from conservative treatment of the condition is an adequate, preserved circulation in the affected area. Preoperative knowledge of the vascular anatomy of the kidneys is also of considerable importance in the surgical approach. An evaluation of the influence of medical treatment is excluded as no repeat angiography has been performed in this material.

Chest films were available in thirty nine of the patients, twenty-eight having changes compatible with tuberculosis. Many of these were only minimal, such as small pleural adhesions or minor calcifications. Eleven of the patients had normal chest films.

## SUMMARY

The results of nephroangiography and urography in 43 patients with renal tuberculosis were analyzed and the value of the two methods was compared. Changes suggestive of tuberculosis more often appeared at urography than at angiography. Urography provided the more detailed information concerning the collecting system while angiography was of decisive importance in the demonstration of the extension of parenchymal lesions.

## ZUSAMMENFASSUNG

Die Ergebnisse bei Nierenangiographie und Urographie in 43 Patienten mit Nierentuberkulose wurden verglichen und der Wert der beiden Methoden wird diskutiert. Veränderungen die auf Tuberkulose deuteten, konnten häufiger mit Urographie als mit Angiographie festgestellt werden. Mit Urographie konnte das Ausscheidungssystem besser dargestellt werden während Angiographie hinsichtlich der Ausbreitung von Parenchymläsionen entscheidend war.



## RÉSUMÉ

Les auteurs ont analysé les résultats et comparé la valeur de l'angiographie rénale et de l'urographie chez 43 malades atteints de tuberculose rénale. L'urographie a montré des signes qui font penser à la tuberculose plus souvent que l'angiographie. C'est l'urographie qui a fourni les renseignements les plus détaillés concernant les voies collectrices de l'urine alors que l'angiographie a une importance décisive pour montrer l'étendue des lésions parenchymateuses.

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## ANGIOGRAPHY IN DUODENAL CARCINOMA

by

OLLE OLSSON

Carcinoma of the duodenum is a fairly rare condition although its true frequency is difficult to estimate from the literature. EGER (1933) gave the frequency as 0.3 per cent of all gastro-intestinal neoplasms, whereas BOCKSTEN (1963) raised the figure by a factor of 10 giving an incidence of 3 per cent. Statistical summaries from the literature were presented by SERANO & McPEAK (1966) and by CRAIG (1969).

MATEER & HARTMAN (1932) classified duodenal carcinomas as superampullary, periampullary and infra ampullary and stated that the second group was the most common. BOSSE & NEELEY (1969), however, considered that most primary duodenal

in ... .. BERGENDAL (1939), inter alios, stressed the fact that it is often impossible to differentiate between primary carcinoma of the duodenum and primary pancreatic carcinoma involving the duodenum. The many diagnostic differentials include ulceration of unusual location and benign tumours of the duodenum as well as inflammatory and vascular lesions. SERANO & McPEAK (1966) reported that under a third of the cases in a material of

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Fig. 1. Normal anatomy. Angiography of the celiac artery, arterial phase. Mainly laterally directed branches feed the duodenum from the gastroduodenal artery.

neoplasms of the duodenum had an established pre-operative roentgen diagnosis, these authors stressed the low rate of cure in malignant duodenal tumours, related this to late diagnosis and proposed "Particular attention must be given to roentgen evidence of deformity or obstruction in the second portion of the duodenum. Earlier surgical intervention may be indicated in the postbulbar bleeding 'ulcer' that does not promptly respond to dietary and medical management. Certainly any lesion demonstrable by roentgen in the third or fourth part of the duodenum warrants surgical exploration."

The author feels that he must protest at surgical exploration of lesions that can be diagnosed correctly by suitable roentgen diagnostic procedures. Investigations into the possibility of diagnosing pancreatic carcinoma by angiography have drawn attention to primary carcinoma of the duodenum, a condition that calls for special procedures.

Angiography may prove valuable as an adjunct to conventional methods of examination of lesions of the alimentary tract. It was therefore performed in a series of cases in which malignancy of the duodenum was suggested, or at least could not be excluded. The investigation was thus broadened to determine the usefulness of angiography in those vague lesions of the duodenal loop the exact nature of which cannot be diagnosed by conventional techniques alone.

*Roentgen anatomy* (Fig 1) The blood supply to the duodenum is as follows. The superduodenal artery from the right hepatic artery sometimes supplies the very first part of the duodenum. The main source of blood supply to the duodenum, however, is from branches from the gastroduodenal artery, these feed the duodenum and the head of the pancreas and form two arcades, one anterior to and the other posterior to the head of the pancreas. The posterosuperior pancreaticoduodenal artery and the anterosuperior pancreaticoduodenal artery join the inferior pancreaticoduodenal artery from the superior mesenteric artery and thus form the two arcades. The variations are many, as described by MICHELS (1955), who pointed out that the duodenum is the only part of the intestinal tract that has a double blood supply, one to its anterior and one to its posterior surface. This supply is formed mainly by several fine branches extending laterally and ventrally from the arcades close to the gastroduodenal artery.

The roentgen anatomy was treated in detail by LUNDEQUIST (1965). He stated that the gastroduodenal artery arises in about 75 per cent of cases from the common hepatic artery, in about 10 per cent of cases from the left hepatic artery and in the remaining cases from the right hepatic or an aberrant hepatic artery or directly from the celiac or the superior mesenteric artery. This is important since the trend in angiographic technique is towards increasing selectivity with catheterization of branches of the second and third order from the abdominal aorta.

*Method of examination* It thus appeared that an investigation of both the celiac artery and the superior mesenteric artery was necessary to investigate relevant vasculature angiographically. A combined examination of these two arteries (OLSSON et coll 1962, BOIJSEN & OLIN 1964) seemed to be the best method. The method of choice in investigating the pancreaticoduodenal arcades angiographically is by selective catheterization of the gastroduodenal artery by a special superselective technique (BOIJSEN 1966) or by the selective injection of adrenalin into the celiac artery immediately before the injection of the contrast medium (BOIJSEN & REDMAN 1967). Adrenalin causes constriction of the hepatic vasculature so that the gastroduodenal artery and the arcade arteries are well and selectively filled. It would appear that the combined simultaneous injection into both arteries is the better method. A supplementary superselective examination is often rewarding, as documented by REUTER (1969).

*Material* The present investigation consisted of angiography in 5 cases of verified primary carcinoma of the duodenum as well as in 3 cases of verified carcinoma of the duodenum and of the pancreas in which the pathologist was in doubt as to whether the growth was primarily in the duodenum or in the pancreas. The material also includes one case of carcinoma of the duodenum and

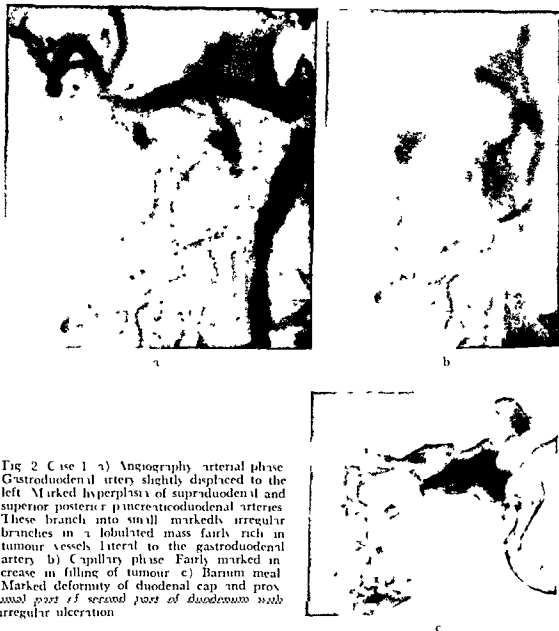


Fig 2 Case 1. a) Angiography, arterial phase. Gastroduodenal artery slightly displaced to the left. Marked hyperplasia of supraduodenal and superior posterior pancreaticoduodenal arteries. These branch into small markedly irregular branches in a lobulated mass fairly rich in tumour vessels lateral to the gastroduodenal artery. b) Capillary phase. Fairly marked increase in filling of tumour. c) Barium meal. Marked deformity of duodenal cap and proximal part of second part of duodenum with irregular ulceration.

the colon, in which no conclusion could be made from the biopsy specimen as to its primary site and finally, for comparison, one case of a recurrence of a carcinoma of the colon encroaching upon the duodenum.

A group of duodenal lesions other than primary carcinoma will be discussed in a paper to follow. This group represents changes which at conventional examination had been given the diagnosis of carcinoma of the duodenum or in which this condition was possible or could not be excluded. The angiographic

changes in these cases will be discussed in relation to the angiographic appearances of primary carcinoma of the duodenum

The 5 cases of patho anatomically verified primary carcinoma of the duodenum consisted of 3 cases investigated with combined and simultaneous celiac and superior mesenteric angiography, one case with selective celiac angiography and superior mesenteric angiography with separate injections of contrast medium and one case examined by celiac angiography alone

# Case reports

*Case 1* Male aged 65 had had stomach trouble for four years with pain in the upper part of the abdomen and had been treated for duodenal ulcer. The pain had increased and on roentgen examination in another hospital marked changes in the duodenal cap prompted a diagnosis of duodenal ulceration. Operation revealed a large ulcerated lesion. Histology demonstrated adenocarcinoma. The patient was transferred to us. Roentgen examination indicated marked changes in the duodenal cap compatible with malignancy (Fig 2c). At angiography (Fig 2b) the gastroduodenal artery was displaced medially and backwards. The hyperplastic and irregular superduodenal artery formed irregular vessels into the lateral part of the tumour (Fig 2c). The posterosuperior pancreaticoduodenal artery was wide and divided into irregular tumour vessels delineating the medial part of the tumour. The mass was best demonstrated in the capillary phase, it had an irregular surface and extended mainly ventrolaterally to the gastroduodenal artery. The diagnosis of carcinoma of the duodenum was confirmed by histology following resection of the tumour.

*Case 2* Female, aged 60 with pain in the right upper part of the abdomen for a short time. Cholecystography revealed gallstones and cholecystectomy was performed. No abnormality was evident in the duodenum. Examination of the cholangiograms in retrospect however, disclosed infiltration of the superpapillary part of the duodenum just above the papilla. A barium meal disclosed moderate stenosis of the second part of the duodenum (Fig 3c) and was presumed to be a malignant condition either of the duodenum or secondary from the pancreas. Angiography (Fig 3 a and b) demonstrated slight displacement of the gastroduodenal artery in a curve medially. The posterosuperior pancreaticoduodenal artery close to its origin was slightly irregular, and in a  $4 \times 2$  cm region near the gastroduodenal artery small tumour vessels were evident. A tumour was well delineated in the capillary phase (arrows, Fig 3b). The splenic and portal veins as well as the dorsal pancreatic artery and anterosuperior pancreaticoduodenal arteries were normal. The diagnosis of carcinoma of the duodenum was confirmed by histology (adenocarcinoma) following resection. The pancreas was not involved.

*Case 3* Male, aged 73 had been suffering from pain in the upper part of the abdomen suggestive of gallstones. Cholecystography. Normal Roentgen examination of the stomach and duodenum. A 6 cm area of infiltration in the middle of the second part of the duodenum with a central  $3.5 \times 1.5$  cm area of ulceration, probably malignant (Fig 4 a and b). Angiography demonstrated marked vascularity corresponding to the infiltration by duodenal branches from the gastroduodenal artery. The arteries were irregular and tumour vessels were present (Fig 4c). The tissue increased in density in the capillary phase. The

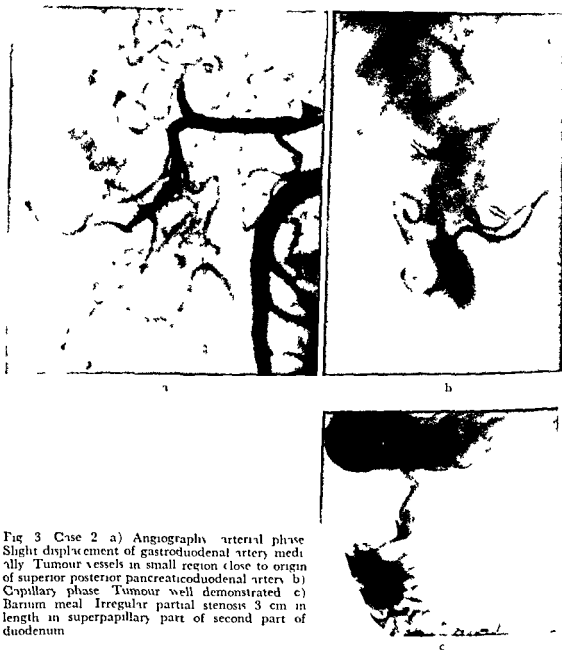


Fig 3 Case 2 a) Angiography arterial phase Slight displacement of gastroduodenal artery medially Tumour vessels in small region (close to origin of superior posterior pancreaticoduodenal artery) b) Capillary phase Tumour well demonstrated c) Barium meal Irregular partial stenosis 3 cm in length in superpapillary part of second part of duodenum

diagnosis of carcinoma of the duodenum was confirmed by histology (highly differentiated adenocarcinoma) following resection (Fig 4d)

*Case 4* Male, aged 47, with continuous pain in the upper part of the abdomen for about one year Vomiting and diarrhea during the month before the examination No loss of weight A barium meal revealed a 4 cm circular area of stenosis in the distal region of the second part of the duodenum (Fig 5a) The diagnosis of carcinoma was confirmed by histology (adenocarcinoma) following resection



Fig 4 Case 3 a) b) Slightly irregular 3.5 cm ulceration in papillary part of second part of duodenum c) Angiography Gastroduodenal artery displaced slightly medially Laterally directed branches irregular Tumour vessels corresponding to site of ulceration d) Angiography of operation specimen Deranged arterial architecture in and around ulceration (below clamp)





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Fig 6 Case 5 a) Dilatation of stomach and duodenum. Marked stenosis 3 cm long in distal part of duodenum. b) Angiography of superior mesenteric artery. First branches laterally markedly irregular by infiltration and displayed downwards in a curve. Many tumour vessels in concavity of curve.

These 5 cases represent all the different sites of carcinoma of the duodenum. The first 4 cases present essentially the same angiographic features. The fifth case, one of a tumour lying distally in the duodenum, differs from the others because the feeding vessels arose exclusively from the superior mesenteric artery. The first 4 cases bore certain characteristic angiographic features. Branches ran directly from the gastroduodenal artery or from the beginning of the pancreaticoduodenal arcades mainly laterally and centrally to form a few tumour vessels. The tumour, lying mainly lateral to the gastroduodenal artery, was well demonstrated in the capillary phase. The dorsal pancreatic and transverse pancreatic arteries were not involved and the arcade arteries, if affected, had changes only in their lateral parts, the splenic and portal veins were unchanged.

Displacement of the arteries, e.g. the gastroduodenal and hepatic arteries was apparent, as usual in angiographic tumour diagnosis, such displacement is of little significance.

It is noteworthy that the recurrence in Case 4, angiographically examined eight months after extirpation of the primary growth, had a much more prom-



Fig 5 Case 4 a) Marked stenosis, 4 cm long, in infrapapillary part of duodenum b) Angiography. Recurrence of primary carcinoma of duodenum. Markedly vascularized tumour in and around head of pancreas, with infiltration of arteries and many tumour vessels

The patient then felt well for 18 months before he again experienced pain. Roentgen examination of the duodenum now demonstrated an expansive growth in the head of the pancreas, pressing upon the second part of the duodenum. Angiography disclosed that the gastroduodenal artery and all the pancreatic arteries were wider than normal in a 7 cm region, corresponding to the head of the pancreas. Tumour vessels were evident in a 3 cm area in the cranial, ventral part of this region (Fig 5b). The diagnosis of recurrence with invasion into the pancreas was confirmed at exploratory laparotomy.

**Case 5** Male, aged 39, with eighteen months history of upper abdominal discomfort. Some vomiting had occurred. A barium meal examination revealed marked dilatation of the stomach and first part of the duodenum, a 3 cm area of narrowing was evident in the distal part of the duodenum (Fig 6a). Exploratory laparotomy disclosed a growth in the duodenum adherent to the aorta and inferior vena cava as well as to the body of the pancreas. Surgically the tumour gave the impression of being a primary pancreatic carcinoma, duodeno-jejunostomy was performed. Biopsy of the tumour suggested metastases from an adenocarcinoma. As the roentgen examination had not been confirmed it was supplemented by angiography with separate injections of contrast medium into the celiac and the superior mesenteric arteries (Fig 6b). The right hepatic artery was seen to stem from the superior mesenteric artery. A tumour, about 7 cm in diameter, fed by the superior mesenteric artery was infiltrating the first jejunal branches and displacing the superior mesenteric artery and vein ventrally (Fig 6b). Many pathologic vessels were present. No changes in the pancreas and no metastases in the liver were evident. A large tumour in the mesentery close to the duodenojejunal flexure and the upper part of the jejunum was resected and proved to be an adenocarcinoma of the duodenum.



Fig 8 Case 7 a) Angiography following adrenalin) Duodenal branches laterally from gastroduodenal artery displaced upwards and medially Distal lateral branches infiltrated Some tumour vessels b) Capillary phase Tumour well outlined c) Barium meal Marked stenosis 2.5 cm long in second part of duodenum.

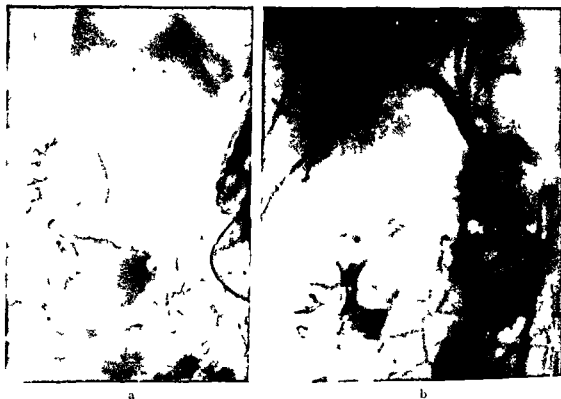


Fig 7 Case 6 a) Large ulcerating tumour in second part of duodenum including the papillary region b) Slight displacement of gastroduodenal artery medially with laterally extending branches irregular. Numerous fine tumour vessels

inent vascularization with marked encroachment upon large arterial branches, above all there was an abundance of tumour vessels, as compared with the scarcity of such vessels in the original tumours. The local recurrence in Case 6 (presented below) had marked vascularity, much more prominent than in the original growth.

The angiographic features were essentially the same in Case 5 except that the origin of the abnormally changed arteries was the superior mesenteric artery.

Conventional roentgen examination suggested primary carcinoma of the duodenum in 3 cases. The angiographic appearances are described below. Histology failed to indicate whether the tumour primarily arose in the duodenum or in the pancreas. Concomitant neoplasms in the duodenum and colon were present in another case.

*Case 6* Female, aged 29 with pain in the right upper part of the abdomen and vomiting for a few months. A barium meal examination revealed infiltration with a large irregular area of ulceration of the second part of the duodenum (Fig 7a). Angiography demonstrated that the gastroduodenal artery was displaced medially (Fig 7b) and the common hepatic

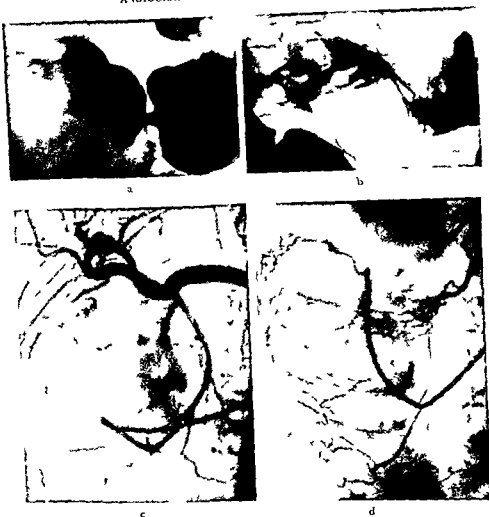


Fig 10 Case 9 a) Irregular stenosing infiltration in proximal part of duodenum. b) Colon Irregular stenosing infiltration 15 cm long c) Angiography of celiac artery. Marked displacement of gastroduodenal artery medially with large tumour rich in tumour vessels in celiac axis d) Angiography of superior mesenteric artery. Branches to right part of colon infiltrated. Many tumour vessels.

**Case 8** Male, aged 60 who had had continuous pain in the upper part of the abdomen and loss of weight for some months. There was a stenosis in the distal part of the duodenal lumen (Fig. 11c). The pancreatic and transverse processes of the pancreas as well as the splenic portal veins were normal. Selective superior mesenteric



Fig 9 Case 8 a) Irregular stenosis 4 cm in length mainly in convexity of duodenal loop and with polypous extension into stenosed lumen b) Angiography of celiac and superior mesenteric arteries Infiltration in medial part of lower pancreaticoduodenal arcade close to main stem of superior mesenteric artery Infiltration of branches to the left of this artery and tumour vessels in a 2 x 3 cm area No pancreatic vessels involved

artery slightly cranially. Several wide branches were directed laterally from the pancreaticoduodenal arteries and from these irregular tumour vessels were filled. The branches were extended and together with the medially displaced gastroduodenal artery and the cranially displaced hepatic artery encircled a large tumour. The diagnosis of carcinoma of the duodenum was confirmed by histology (adenocarcinoma of the duodenum and pancreas probably primarily in the former). The pancreas and duodenum were partly resected and partial gastrectomy and gastroenterostomy performed.

Eight months later further combined celiac and superior mesenteric angiography was carried out to check the operation result. No pathologic vasculature was evident. Angiography of the right renal artery was undertaken for exploration of the retroperitoneal space. A neoplasm rich in tumour vessels lay medially and cranially to the right kidney; this was displaced and the ventral branch of the right renal artery was compressed and infiltrated.

**Case 7** Female aged 34 who a few years previously had had severe pain in the upper part of the abdomen to suggest gallstone colic. Cholecystography Normal. A barium meal examination revealed a 2.5 cm area of stenosis in the second part of the duodenum. Celiac angiography indicated that the gastroduodenal artery was normal. Wide branches extended from the middle of the artery in cranial, lateral and ventral directions and diminished in size as they became tumour vessels. A mass localized laterally and caudally to the gastroduodenal artery was outlined in the capillary phase (Fig 8 a and b). The dorsal pancreatic artery and the arcade arteries as well as the splenic and portal veins were normal. The diagnosis of carcinoma of the duodenum was confirmed by histology (adenocarcinoma). Its primary site was not obvious.

Doubt existed in 2 of the above 4 cases whether the neoplasm in the duodenum was primarily duodenal or pancreatic. A review of the microscopy changes in one of the cases, however, suggested that the tumour had arisen in the duodenum. In the third case the diagnosis of carcinoma was made from the biopsy specimens but the origin could not be determined. All 3 cases exhibited changes at conventional examination and angiography and the pancreas was involved. No changes compatible with those evident in the large material of angiography in pancreatic carcinoma were however present. The cases therefore all belong angiographically to the primary duodenal carcinoma group, and there was nothing in the histology to suggest otherwise.

In the fourth case it was impossible to decide by histology whether the neoplasm had arisen in the duodenum or in the colon. Angiographically the changes in the duodenum were the same as those present in primary carcinoma of the duodenum. Those in the colon were however of the same nature and corresponded to changes evident in the material of angiography in primary carcinoma of the colon (BOIJSEN & REUTER 1966).

A patient with an extension to the duodenum of a primary carcinoma of the colon was examined.

*Case 10* Male, aged 63, who four months earlier had been operated upon at another hospital for carcinoma of the ascending colon: this infiltrated the duodenum and radical removal was considered impossible at that time. The patient was transferred to us. A barium examination disclosed irregular infiltration of the second part of the duodenum with some stenosis and a small area of ulceration (Fig 11a). Selective celiac angiography revealed innumerable small metastases in the liver (Fig 11b). Selective superior mesenteric angiography demonstrated wide pancreaticoduodenal arteries (Fig 11b). Small irregular arterial branches extended caudally and laterally from the caudal part of the lower arcade into tumour vessels. A lobulated 6 cm mass was demonstrated in the capillary phase.

The tumour vessels were apparent only at superior mesenteric angiography, in spite of the fact that the arcade arteries were filled at celiac angiography. The metastases in the liver contraindicated surgical intervention.

The angiographic changes in this case do not differ from those in a primary growth of the duodenum. Thus if the neoplasm infiltrates both a part of the colon and an adjacent part of the duodenum, it seems impossible to decide angiographically in which part of the bowel the tumour has its primary site.

In summary, a material has been presented of nine cases with an angiographic diagnosis of carcinoma of the duodenum. The tumour in 3 cases was supra-ampullary, in 3 periampullary and in 4 cases it had an infra ampullary localization. At conventional examination the roentgenologic features differed markedly, the growth exhibiting irregular or regular, small or large areas of ulceration, more widespread irregular infiltration or produced well defined marked stenosis of the duodenal lumen. Six of the cases had histologic evidence of being primary





Fig 11 Case 10 a) Slight infiltration in second part of duodenum with small distal area of ulceration b) Angiography of celiac and superior mesenteric arteries Stenosis at mouth of celiac artery Filling by wide collaterals over pancreaticoduodenal arcades Infiltrated branches laterally with tumour vessels corresponding to second part of duodenum

angiography revealed that the most medial part of the lower arcade was irregular and that some small tumour vessels were filled. A duodenal arterial branch to the left arising from the beginning of the superior mesenteric artery was irregular and led to a 2 cm area in which a large number of pathologic vessels were present. A diagnosis of carcinoma of the duodenum was confirmed by histology (anaplastic adenocarcinoma).

**Case 9** Female, aged 56 with melena. Cholecystography. No filling of gallbladder. Cholegraphy. Bile ducts of normal width, medium passed to the duodenum. A barium examination demonstrated irregular stenosis of first part and upper end of the second part of the duodenum (Fig 10a). Selective celiac followed by mesenteric superior angiography (Fig 10, c and d) revealed a mass 15×20 cm in size extending from the lower part of the liver to the crest of the right ileum. The tumour received its arterial supply from the gastroduodenal artery, which was displaced to the left, as well as from the cystic artery. The lower part of the neoplasm was supplied from the right colic artery and from the medial colic artery. A great number of tumour vessels were present. These findings suggested a roentgen examination of the large bowel at which a stenosis 15 cm long was present in the proximal part of the transverse colon and the hepatic flexure (Fig 10b). Exploratory laparotomy disclosed a large tumour probably arising from the colon and encroaching upon the duodenum and the liver, with metastases in the latter. Low differentiated carcinoma was confirmed by histology.

Angiography of lesions of the duodenum would appear to be a rational procedure when conventional methods prove insufficient

# SUMMARY

A material of 9 cases of carcinoma of the duodenum examined by angiography is presented. This consisted of 5 verified cases: 3 of carcinoma of the duodenum or pancreas and cases of carcinoma of the duodenum, pancreas or colon. It is suggested that the number of cases of primary duodenal carcinoma may be greater than usually believed.

# ZUSAMMENFASSUNG

Ein Material von 9 Fällen von Carzinom im Duodenum wurde angiographisch untersucht. Fünf dieser Fälle wurden pathologisch bestätigt: in drei war der Ursprungsort entweder im Duodenum, im Pankreas oder im Colon. Es erscheint durchaus möglich, dass sich primäre Duodenalkarzinome häufiger ereignen als man bisher geglaubt hat.

# RÉSUMÉ

L'auteur présente 9 cas de cancer du duodénum examinés par angiographie. Ils comprennent 5 cas vérifiés: 3 de cancer du duodénum ou du pancréas et des cas de cancer du duodénum, du pancréas ou du colon. L'auteur pense que les cas de cancer du duodénum sont plus fréquents qu'on ne le croit généralement.

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carcinoma of the duodenum whereas in 3 cases doubt existed as to whether the tumour was primary in the duodenum or the pancreas (2 cases) or the colon (1 case). Angiographically the cases had similar features distinctly differing from those in pancreatic carcinoma but corresponding to those in others parts of the small and large intestines.

### Discussion

The diagnosis as to the exact nature of primary carcinoma of the duodenum is difficult and often impossible by the use of conventional methods alone. Such a diagnosis is important because of therapeutic considerations. A benign lesion, for example an ulcer at an unusual site, may usually be treated conservatively. If or a malignant lesion, surgery represents the rational therapy and infers radical resection in a region which includes the bile ducts and the pancreas.

Angiography of the celiac and the superior mesenteric arteries was employed in order to improve the diagnostic acumen. The cases of duodenal carcinoma of the duodenum described demonstrated vascular changes of a fairly characteristic type. The duodenal branches were affected by infiltration and newly formed tumour vessels, usually lateral to the gastroduodenal artery, were demonstrable. The gastroduodenal artery was not involved except for being displaced to the left and ventrally, the pancreaticoduodenal arcade arteries immediately adjacent to the latter or the superior mesenteric artery were sometimes involved.

Branches of the superior mesenteric artery are affected in a corresponding way when the growth is situated in the lower parts of the duodenum. The tumour is fairly well outlined in the capillary phase but the vascular pattern is different as compared with carcinoma of the head of the pancreas. The changes in pancreatic carcinoma are medial to the gastroduodenal artery. This artery is often involved, as are the dorsal pancreatic and the transverse pancreatic arteries, and in the capillary phase the tumour is usually less well demonstrated.

The frequency of primary carcinoma of the duodenum is important. Five cases of carcinoma of the duodenum have been presented in this paper. In addition 3, possibly 4, cases of carcinoma of the duodenum with involvement of the pancreas or the colon were probably unproved cases of primary growths of the duodenum.

Some of the cases in which doubt exists as to whether the tumour is a primary carcinoma of the duodenum or a carcinoma of the head of the pancreas extending into the duodenum, may arise primarily in the duodenum and only secondarily affect the pancreas. Accordingly, the percentage of cases of carcinoma of the duodenum may be much higher than the figures given in the literature. There seems to be no possibility of differentiating angiographically between a primary carcinoma of the duodenum and one arising in another part of the bowel.

## ARTERIOGRAPHIC INVESTIGATIONS OF THE NORMAL HIP IN ADULTS

Evaluation of methods and vascular findings

by

H MUSSBICHLER

Arteriographic investigations of the normal hip *in vivo* have been published by MUSSBICHLER (1956), HIPPE (1962) and BRUGGER (1963). However, the patient materials were comparatively small and the technique employed was rather primitive compared to modern standards. Moreover, these investigations were not carried out to evaluate anatomic details.

Recent developments in angiographic techniques, such as the use of catheters, film changers and the subtraction method, have made possible far more detailed and reliable demonstrations of the arteries. These methods have been used in the present investigation, the aim of which was to study the filling frequency, origin, course and ramifications, as well as atherosclerotic changes, in the more important arteries of the clinically unaffected hip region.

The gross anatomy of the arteries of the hip (Fig. 1) was investigated in human cadavers by NUSSBAUM (1926), TUCKER (1949), WOLCOTT (1943), HOWE & SCHWARTZ (1950), HULTH (1953) and HIPPE (1962). Their results may be summarized as follows:

The femoral head is supplied by the posterior collum branch of the medial

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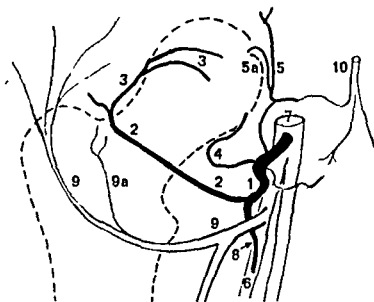


Fig. 1 Arteries of the hip region. 1 — Medial circumflex artery, 2 — Posterior collum branch (MUSSBICHER 1956) ramus profundus (PNA 1955) 3 — Superior retinacular artery (TUCKER 1941) ramus nutritius capitis superiores (MUSSBACH 1926, PNA 1955), posterior superior capital branch (HOWE & SCHWARTZ 1950), superior epiphysal artery (TRUETA & HARRISON 1953), 4 — Inferior retinacular artery (TUCKER 1941) ramus nutritius capitis inferiores (MUSSBACH 1926, PNA 1955), posterior inferior branch (HOWE & SCHWARTZ 1950) inferior metaphysal artery (TRUETA & HARRISON 1953) 5 — Acetabular artery 5a — Ligamentum teres artery = medial epiphysal artery (TRUETA & HARRISON 1953) 6 — Deep femoral artery, 7 — Inferior branch of the medial circumflex artery 8 — Inferior branch of the lateral circumflex artery, 9a — Superior branch of the lateral circumflex artery, 9a — Superior branch

circumflex artery. This runs along the posterior aspect of the neck, traversing the joint capsula, to the intertrochanteric notch where it gives off the superior retinacular artery, this courses along the neck to the epiphysal part of the caput. On the lower side of the femoral neck the medial circumflex artery gives off the inferior retinacular artery which runs in the distal part of the capsula and periosteum to the lower part of the head. The artery of the teres ligament arises from the acetabular artery and runs within the ligament to the foveal area of the caput.

Microangiographic investigations in human specimens (TRUETA & HARRISON 1953, SEWITT & THOMPSON 1965) revealed that the superior retinacular artery is the main vessel of the femoral head while the inferior retinacular artery and the ligamentum teres artery supply only a small distal part of the caput and the foveal area, respectively. Moreover, SEWITT & THOMPSON demonstrated that transection of the inferior retinacular and ligamentum teres arteries did not reduce the vascularisation of the caput while transection of the superior retinacular artery interfered with the filling of the intraosseous vessels of the caput.

Table 1  
*Age distribution in the series of 97 cases*

|                 | Age in years |       |       |       |       |       |
|-----------------|--------------|-------|-------|-------|-------|-------|
|                 | 30—39        | 40—49 | 50—59 | 60—69 | 70—79 | 80—89 |
| Number of cases | 4            | 10    | 27    | 38    | 14    | 3     |

in 27 out of 28 specimens. Only in one case was this interference compensated by ramifications of the inferior retinacular artery.

*Material.* This comprised 'normal hips' from 97 subjects thirty seven of whom were examined primarily by selective nephroangiography and only secondarily by angiography of the hip. The 'normal hip' was in 60 subjects examined in connection with angiography of the contralateral hip which was affected by fracture, necrosis or arthrosis.

'Normal hips' were characterized by the absence of symptoms and of pathologic, clinical and roentgenologic signs, small osteophytes alone were not considered pathologic in this connection. The age distribution is given in Table 1.

## Methods

### *A General arteriography in 63 cases (Fig 2a)*

This method was based on retrograde injection of contrast medium into the common femoral artery either by the blunt Seldinger cannula or a catheter. With the former procedure (15 cases) four a.p. films were obtained during and after injection of 20 ml. Diodon 50 % and in the latter procedure (48 cases) 16 ml. Urografin 76 % were injected through a 60 cm. polythene catheter No. 205, and serial exposures were made. The leg was fixed by a broad band on the examination couch. The injection time was about 2 to 3 seconds.

### *B Semiselective arteriography in 29 cases (Fig 2b)*

An amount of 10 ml. Urografin 76 % was injected in a distal direction into the common femoral or deep femoral artery. This was achieved by insertion in a distal direction of a straight polythene catheter in 3 cases (Figs 4 and 8) and by using a red Ödman-Ledin catheter in 26 cases (Figs 3 and 11). The tip of the latter catheter was formed into a reversing loop of about 1 cm. in width and 2.5 cm. in length, and the catheter was inserted percutaneously into the femoral artery.



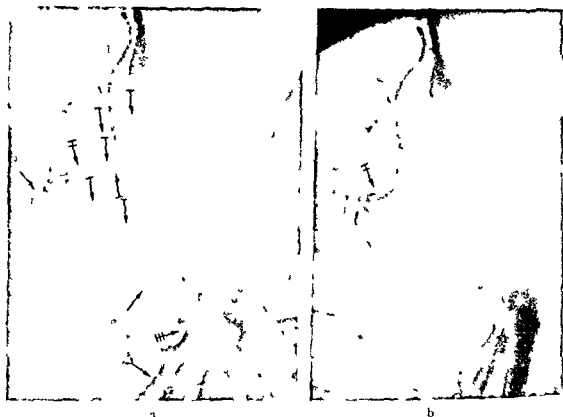


Fig. 2 Case examined by both general (a) and semiselective (b) arteriography. In (a) the gluteal branches (→) are superimposed on the femoral head and its vessels, particularly the superior retinacular artery (→→) while in (b) the filling is limited to the external iliac artery and its branches. Posterior collum branch (→) arises at the bifurcation (→→) of the medial circumflex artery together with the inferior branch (→→).

and pushed up into the aorta. By introducing the loop into one of the aortic branches it became directed downwards and re-assumed its looped form. At this stage the loop returned to the aorta and with rotational movements was pulled downwards to the common femoral artery just proximal to the origin of the medial circumflex artery. This procedure, the first part of which was identical with selective catheterisation of aortic branches, was carried out under roentgen TV control and test injections.

### *C Selective internal iliac arteriography in 14 cases (Figs 13 and 14)*

Nine of the cases were part of the patient materials examined by methods (A) and (B). The aim of the selective examination was to study whether and to what extent the branches of the internal iliac artery participate in the vascularisation of the hip. The examination was carried out with the same loop-formed Ödman-Ledin catheter as was used in semiselective arteriography. The tip of the catheter



Fig 3 Semiselective arteriograms in 40°  
(  
coll  
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was placed in the trunk of the internal iliac artery by rotating the loop medially on its passage through the common iliac artery. This procedure was also performed under roentgen control and with test injections. Arteriography was carried out with 10 ml Urografin 76 % injected in 1.5 to 2 seconds. This method was first tried out by ÖDMAN (1957) and was later used as a routine in examination of the vascular anatomy of the urinary bladder (NILSSON 1967).

#### *General data*

In all cases except in those 15 cases examined with the Seldinger cannula (method A) serial angiography with one exposure per second over 15 seconds was performed in two positions: internal and external rotation of the hip joint. Two side holes within 2 cm from the tip were made in all catheters. The exposure data were: 60 to 80 kV, 64 mAs and 0.1 second at 100 cm FFD.

The inner diameter of the main arteries was measured by means of a 5 times magnification glass with a built-in millimeter scale.

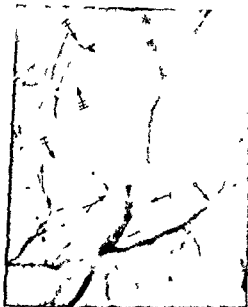


Fig. 4. Subtraction angiogram from a semisel-  
ective examination with a polythene catheter. Ex-  
cepting the superior retinacular artery, all other  
femoral head vessels filled: posterior collum  
branch ( $\rightarrow$ ), inferior retinacular artery ( $\rightarrow$ ),  
acetabular ( $\rightarrow$ ) and ligamentum teres artery  
( $\rightarrow$ ) from the acetabular branches ( $\rightarrow$ ,  $\rightarrow$ ) of  
the obturator and medial circumflex arteries,  
respectively.

### Complications

A thrombo-embolus, which made operation necessary, occurred after the examination in a case with extensive atherosclerotic changes in the arteries. An embolus, which was 20 cm in length, was removed from the femoral artery in Hunter's canal. The postoperative course and the recovery of the patient were without complications. Spasm of the external iliac artery was observed in a woman when the loop of the red Ödman-Ledin catheter became fixed in the artery. The examination was interrupted but the catheter could be withdrawn without difficulty after it had been pushed back to the aortic bifurcation where the loop straightened. It is more than possible that the spasm was caused by the catheter having a too wide loop in relation to the lumen of the external iliac artery. The examination was accomplished with a polythene catheter.

No other complications occurred in this material.

### Results with arteriography of the hip, methods (A) and (B)

The findings in arteriography of the hip, methods (A) and (B), in the 92 cases examined will be described in systematic order and the incidence of atherosclerotic changes will be recorded.

#### *Medial circumflex artery*

This artery was filled in all the ninety-two cases.

It originated from the common femoral artery (Fig. 3) in 19 cases (20%). In three of these the origin was located up to 5 cm proximal to the bifurcation.



Fig 5 Arteriograms with internal (a) and external (b) rotation of the hip joint demonstrating the extension of the posterior collum branch ( $\rightarrow$ ) which is not influenced by the different positions. The superior retinacular artery at the neck ( $\leftrightarrow$ ) is masked by dense bone structure in outward rotation (b). soft tissue branch ( $\rightarrow\rightarrow$ ) the superior branch ( $\rightarrow\rightarrow\rightarrow$ ) from the lateral circumflex artery is in close contact with the posterior collum branch. obturator artery ( $\rightarrow$ )

(Figs 6 and 7b, 7c) and in one case the artery arose from a common trunk together with the inferior epigastric artery

It originated from the deep femoral artery in 18 cases (20%). In two of these, it arose from a common trunk together with the lateral circumflex artery

The origin was close to the bifurcation of the common femoral artery (Fig 7a) in 55 cases (60%). This group comprised all cases in which the exact origin could not be decided, whether from the common femoral or the deep femoral artery

The inner diameter of the medial circumflex artery at 1 to 2 cm from its origin varied between 2 and 4.5 mm. The artery terminated in bifurcating into the posterior collum and the inferior branch (Figs 3 and 9) just above the level of the lesser trochanter. The length of the medial circumflex artery was mainly determined by its point of origin

With respect to its course and ramifications, the medial circumflex artery usually ran in two or three sharp curves in dorsal direction giving off the following important branches: (1) acetabular branch, (2) inferior retinacular artery, (3) posterior collum branch, (4) inferior branch (Figs 2 and 3), and (5) medial branches to the adductor and obturator regions (Fig 3). Of all these branches

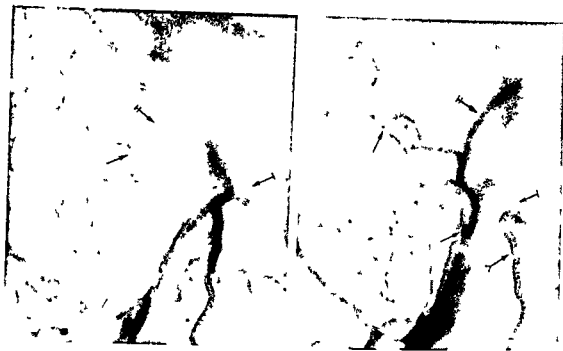


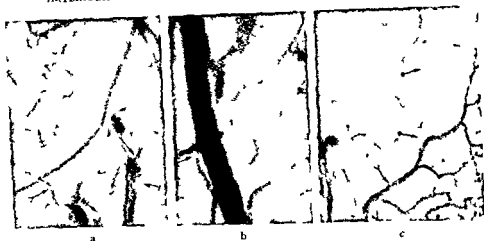
Fig. 6 General arteriography in different circulatory phases and positions. The medial circumflex artery ( $\rightarrow$ ) arises high up from the common femoral artery; the posterior collum branch ( $\rightarrow$ ) of ectopic origin is filling distally from an inferior gluteal branch ( $\leftrightarrow$ ); inferior branch ( $\rightarrow$ ) of the medial circumflex artery.

only (1), (2) and (3) participated in the supply of the femoral head and will be discussed in detail below.

1 The *acetabular branch* (Figs 3, 4, 8 and 11) filled in 20 % of all cases and arose usually as the first branch from the medial circumflex artery. Its width was about 1 mm or less. Its course was directed to the notch of the acetabulum. On its way it usually joined the acetabular branch from the obturator artery (Fig. 4). Both branches, or sometimes only one of them, made up the acetabular artery at the acetabular notch.

The acetabular artery (Figs 3, 4 and 8) arose in the notch of the acetabulum and filled in 25 cases (40 %) in conventional and in 8 cases (27 %) in semi-selective arteriography. The difference between these figures was due to the fact that the tributaries of the acetabular artery mostly arose from the obturator artery and, to a lesser degree, from the medial circumflex artery. The obturator artery (Fig. 5) itself arose mainly from the internal iliac and to a lesser extent from the external iliac artery.

The course of the acetabular artery was directed upwards to the superior surface of the acetabulum, where it ramified into small, inconstantly filled



lateral branch arises high up from the common femoral artery c) In the subtraction view are seen the ascending branch ( $\rightarrow$ ) of the lateral circumflex artery and its superior branch ( $\hookrightarrow$ ) which possibly serve for the absent posterior collum branch

branches The width of the artery at its origin was about 1 mm or less A branch given off just beyond the acetabular notch in two cases ran somewhat laterally to the acetabular artery upwards to the fovea of the femoral head It obviously represented the artery of the teres ligament (Fig 4)

2 The *inferior retinacular artery* (Figs 4 and 9) filled in 58 cases (63 %) It arose usually from the middle part of the medial circumflex artery In one case it came from the obturator branch of the medial circumflex artery and in another from the lateral circumflex artery (which in turn had arisen from a common trunk together with the medial circumflex artery) The inferior retinacular artery was identified by its course which was more or less parallel to the medial border of the femoral neck and directed to the medial lower section of the head The artery then usually divided into two or three small branches

The inferior retinacular artery was rather small, i.e. about 0.5 to 1.0 mm in diameter and relatively often superimposed by other vessels and therefore sometimes difficult to identify

3 The *posterior collum branch* arose 'normally', i.e. at the bifurcation of the medial circumflex artery, in 81 cases (88 %), laterally it formed almost a right



Fig. 8. Semiselective arteriography performed by insertion of a polythene catheter distally (→). Hypoplastic posterior collum branch (⇔) which ramifies (→) and terminates atypically far from the trochanteric notch. The acetabular artery (≡) arises from the acetabular branch (○•) of the medial circumflex artery (→).

angle with the inferior branch. Both branches made up the bifurcation of the medial circumflex artery (Figs 2, 3 and 9).

In 11 cases, however, in contradiction to the descriptions of the anatomists quoted, the posterior collum branch was not made up of a part of the medial circumflex artery. In 2 of these cases its origin was revealed by conventional as well as by selective internal iliac arteriography to be in the inferior gluteal artery (Figs 6 and 14, respectively). In the remaining 9 cases the artery was not filled at all. The other branches of the medial circumflex artery, especially its inferior branch, were well demonstrated (Fig. 7). Non-filling of the posterior collum branch must therefore be due to an anomaly and not to a technical error. In eight of these nine cases, the contralateral hip was also examined. This examination indicated that the posterior collum branch was not derived from the medial circumflex artery in as many as seven cases, in three of which its ectopic origin was found to be respectively in the obturator, lateral circumflex and inferior gluteal arteries.

In one case an accessory posterior collum branch (Fig. 3) arose from the common femoral artery. In three cases the branch was considered hypoplastic because it was generally small and ramified in small atypical branches before it reached the intertrochanteric notch (Fig. 8).

Angiography with the hip in internal and external rotation (Figs 5 and 9) illustrated the course of the posterior collum branch on the dorsal aspect of the

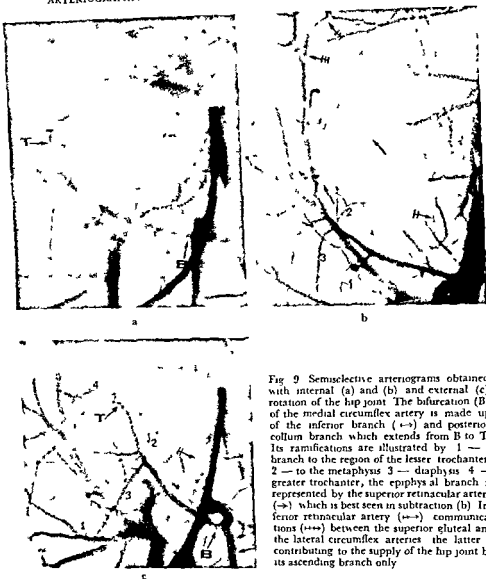


Fig 9 Semiselective arteriograms obtained with internal (a) and (b) and external (c) rotation of the hip joint. The bifurcation (B) of the medial circumflex artery is made up of the inferior branch ( $\leftrightarrow$ ) and posterior collum branch which extends from B to T. Its ramifications are illustrated by 1 — a branch to the region of the lesser trochanter, 2 — to the metaphysis, 3 — diaphysis, 4 — greater trochanter, the epiphyseal branch is represented by the superior retinacular artery ( $\rightarrow$ ) which is best seen in subtraction (b). Inferior retinacular artery ( $\leftrightarrow$ ) communications ( $\leftrightarrow$ ) between the superior gluteal and the lateral circumflex arteries, the latter is contributing to the supply of the hip joint by its ascending branch only.

neck. The different rotational positions of the hip joint actually failed to influence the total extension of the posterior collum branch in the angiogram.

The following ramifications, most of them shown in Fig 9, were observed.

Inconstantly filled small branches to (1) the lesser trochanter, (2) metaphysis,



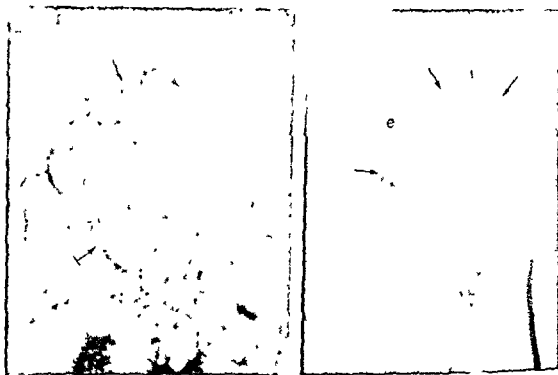


Fig 10 Subtraction angiograms from different circulatory phases illustrating the extra (e) and intra- (i) osseous extension of the superior retinacular artery (→), posterior collum branch (↘)

(3) femoral diaphysis, (4) greater trochanter, and (5) soft tissue close to the trochanteric fossa (Fig 5)

The *superior retinacular artery* was the most constantly filled of the ramifications. Out of the ramifications of the posterior collum branch only the superior retinacular artery participated in the supply of the epiphysal part of the femoral head. The superior retinacular artery (Figs 2, 5 and 10) filled in 63 cases (81 %) of the 78 cases in which the posterior collum branch was normal in origin and size. It did not fill in any of the 14 cases in which the posterior collum branch was not filled, was of ectopic origin, or was hypoplastic.

The superior retinacular artery arose at the trochanteric notch and was located at the upper lateral border of the femoral neck. It was best visible with internal rotation of the leg, in which position it was turned free from skeletal structures, with external rotation it was projected more medially and was superimposed by bone structures (Fig 5b). The artery started its intraosseous course at the level of the epiphysal-diaphysal junction by deviating medially and running in an arch to the center of the head (Fig 10). The intraosseous extension was demonstrated to a greater or lesser extent in 19 cases while in the remainder only the extraosseous part of the artery filled to an individually varying extent.

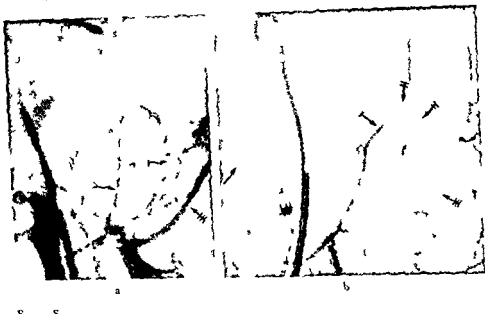


Fig. 1. a) Lateral circumflex artery; b) Medial circumflex artery. Arrows (→) point to the lateral circumflex artery and acetabular branch (→) of the medial circumflex artery.

The artery in single cases branched shortly after its origin into two vessels which ran more or less parallel directed to the center of the head. However as the diameter of these branches was very small they were not suitable for detailed angiographic investigations. The trunk of the superior retinacular artery at the neck in no case exceeded 1 mm in diameter and was usually considerably smaller.

4. *The inferior branch of the medial circumflex artery.* Though not named in the literature the recognition of this branch was of great help in the identification of the posterior collum branch. It always filled and represented both in caliber and course the continuation of the medial circumflex artery. The inferior and posterior collum branch formed the bifurcation of the medial circumflex artery, the inferior branch (Fig. 1, b) and the posterior (Fig. 1, c) and 14).

#### *Lateral circumflex artery*

This artery filled in all 92 cases. It arose at various levels from the deep femoral artery except in two instances in which it arose from a common trunk together with the medial circumflex artery.

Fig. 12 a) Extensive calcification in the wall of the medial circumflex artery ( $\leftrightarrow$ ) and the posterior collum branch ( $\rightarrow$ ) in male, aged 71 years without signs in the hip b) Another patient in whom angiography revealed atherosclerotic occlusion of the femoral artery as well as stenosing plaques at the bifurcation ( $\rightarrow$ ) of the medial circumflex artery, involving the posterior collum branch and inferior branch as well as the lateral circumflex artery at ( $\leftrightarrow$ )



The lateral circumflex artery gave rise at the lesser trochanter to the ascending branch (Figs 7, 9 and 11). Only this branch participated in the supply of the femoral region. It ran almost parallel with the trochanteric line at the anterior aspect of the neck to the greater trochanter where it ramified. Some branches, the recognition of which seemed important were given off on the way.

*Soft tissue branches* (Figs 11 and 14). These filled inconstantly and varied individually in location and number. They usually crossed the femoral neck and head and coursed to the soft tissue laterally and anteriorly to the hip joint. As these branches may simulate the posterior collum branch and superimpose upon the femoral head vessels their recognition is essential.

The *superior branch*, unnamed in the literature, was present in 70% of the cases. The branch usually arose from the first third of the ascending branch and ran laterally upwards to the trochanteric notch where it was in close contact with the posterior collum branch (Figs 5, 7c and 11). The superior branch may contribute to the supply of the femoral head and possibly serve for the posterior collum branch in cases in which this is not filled (Fig 7, b and c). Anastomoses between the two branches, described in the anatomic literature, could not be proved angiographically, probably due to the small diameter of the vessels.

### *Organic arterial changes }*

Stenosing atherosclerotic plaques of varying size were observed in the external iliac artery and its branches in 22 cases, in 10 of which the medial circumflex

Table 2

*Frequency of filling of the superior and inferior retinacular arteries and the acetabular artery demonstrated by general and semiselective arteriography*

| Artery filled        | Arteriography      |      |                          |      |
|----------------------|--------------------|------|--------------------------|------|
|                      | General (63 cases) |      | Semiselective (29 cases) |      |
| Superior retinacular | 43                 | 69 % | 20                       | 70 % |
| Inferior retinacular | 39                 | 62 % | 19                       | 65 % |
| Acetabular           | 25                 | 40 % | 8                        | 27 % |

artery and in 7 the posterior collum branch was also involved. In 2 cases, extensive calcifications in the wall of the arteries were visible in conventional films (Fig 12a). Large atherosclerotic plaques at the origin of the posterior collum and the inferior branch as well as in the lateral circumflex artery are shown in Fig 12b. The figures indicate that there were no skeletal changes in the hip, the patient had no symptoms.

#### *Comparison of general and semiselective arteriography*

In order to test the efficiency of general and semiselective arteriographic methods the frequency of the filling of the femoral head vessels was compared from the two materials (Table 2).

General arteriography concerned 63 and semiselective arteriography 29 cases. It appears from Table 2 that the filling frequency was practically the same in both materials as concerns the superior and inferior retinacular artery. The acetabular artery, however, filled more frequently with the general (40 %) than with the semiselective (27 %) method. This is due to the fact that general arteriography leads to a filling of the internal iliac artery. This contributes, according to generally recognized anatomic conditions, to the filling of the acetabular artery via the obturator artery to a larger extent than via the medial circumflex artery.

#### **Results with selective internal iliac arteriography, method (C)**

The purpose was to find out whether and to what extent the branches of the internal iliac artery were participating in the supply of the femoral head by anastomoses or aberrant (ectopic) vessels.

Anastomoses were observed in 3 cases (Fig 13). In all of them the posterior collum branch filled from the inferior gluteal artery via its soft tissue branch on

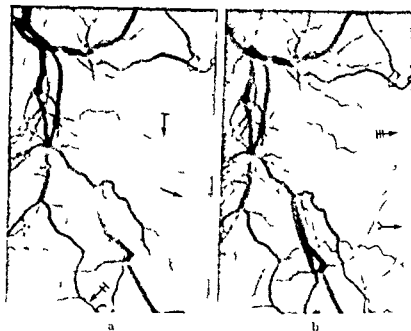


Fig. 13 Subtraction angiograms from selective internal iliac arteriography in the early and mid arterial phases a) Anastomoses from the inferior gluteal artery ( $\longleftrightarrow$ ) to the posterior collum branch ( $\rightarrow$ ) and from the obturator to the medial circumflex artery at ( $\longleftrightarrow$ ) b) Anastomoses between the superior gluteal ( $\longleftrightarrow$ ) and lateral circumflex ( $\rightarrow$ ) arteries

the lateral proximal aspect of the hip joint. In these three cases the trunk of the medial circumflex artery also filled by anastomoses from the obturator artery. In one of the cases anastomoses were present also between the superior gluteal and lateral circumflex arteries. In the remaining 11 cases no communications from the branches of the internal iliac and the circumflex arteries were recognized.

**Femoral head vessels.** The acetabular artery filled in 6 cases (43%) while the superior or inferior retinacular artery was not demonstrated in any one of the cases.

The *posterior collum branch* filled from the inferior gluteal artery ectopically in one case (Fig. 14).

### Discussion

Arteriography of the normal hip has been carried out previously. Contrast medium has been injected into the common femoral artery through the blunt Seldinger cannula by MUSSBICHLER (1956), and through a long sharp needle by



a

Fig 14 Case examined both with semiselective (a) and selective internal iliac arteriography (b) and (c) The posterior collum branch ( $\rightarrow$ ) does not arise from the medial circumflex artery ( $\leftrightarrow$ ) but ectopically from the inferior gluteal artery ( $\leftrightarrow\leftrightarrow$ ) The inferior branch ( $\times\rightarrow$ ) of the medial circumflex artery and the soft tissue branches ( $\rightarrow$ ) from the lateral circumflex artery should not be confused with the posterior collum branch



b



c

HIPP (1962) and BRUGGER (1963) Three to four films were obtained in one position only

The use of needles may cause lesions of the arterial wall particularly if movements of the hip cannot be wholly eliminated as is always the case when the examination for some reason is protracted The use of a blunt cannula is less dangerous Needles and cannulas often mask parts of the vessels Another important disadvantage is that they do not permit internal and external rotations of the hip joint Such examinations in different positions are useful, and sometimes needed in order to obtain a reliable identification of vessels In the present investigation needles and cannulas were replaced by catheters, serial exposures were made with an automatic film changer, and the subtraction method was applied

Two modifications of the catheter method were used in the examination of

vessels of the hip joint. The first method with contrast injection into the common femoral artery in retrograde direction is called 'general arteriography' because the internal iliac artery is also filled. The second method, consisting of injection into the same artery in an antegrade direction, is termed 'semiselective arteriography' as contrast medium is directed to the circumflex arteries, and filling of the gluteal vessels and their superimposition on the vessels of the head of the femur is avoided. Apart from an increased frequency of filling of the acetabular artery by general arteriography, both methods are equal as regards filling of the other femoral head vessels. Semiselective arteriography is, however, superior as regards the selectivity of the filling of the arteries of the hip.

The contribution of the internal iliac artery to the vascular supply of the femoral head is, under normal conditions, restricted to the acetabular (ligamentum teres) artery and to small inconstantly present anastomoses to the posterior collum branch. Selective filling of the internal iliac artery is valuable in detecting the ectopic origin in cases in which the posterior collum branch did not arise from the medial circumflex artery.

The use of the red Ödman-Ledin catheter, with the loop that can be inserted at any level, permits all three types of examination, general, semiselective and selective internal iliac arteriography. However, it presupposes the availability of a roentgen TV-unit and, not least, some experience in selective catheterisation.

Previous arteriographic examinations of healthy hips were made only for comparative investigations with angiograms from fractures or necrosis of the femoral head. They confirm features of the vascular anatomy described in anatomic publications but make no contribution to the evaluation of the vascular anatomy. Both MUSSBICHLER (1956) and BRUGGER (1963) found that filling of the femoral head vessels did not occur in all cases examined. MUSSBICHLER reported filling of the inferior retinacular artery in 13 of his 15 cases. BRUGGER, in his material of 21 cases, observed constant filling of the inferior retinacular artery, filling of the superior retinacular artery in 4 cases, of the acetabular artery in 13 and the ligamentum teres artery in one case. HIPPE (1962) illustrated and described angiograms of some individual cases but did not specify his material nor the results of his examination.

The present investigation indicates that many individual variations in filling frequency and vascular anatomy occur. These concern anomalies of the posterior collum branch, such as hypoplasia, failure of filling from the medial circumflex artery and ectopic origin. As the former condition was not due to technical errors it must be classified as an anomaly of the origin of the posterior collum branch. The possibility cannot be excluded that the origin was ectopic though not detected, or that the artery was replaced by another vessel. The latter condition has been observed in medial neck fractures by BRUNNER, CHRISTIANSEN & KRISTENSEN

(1967) and MUSSBICHLER (1970) In the cases described, the superior branch from the lateral circumflex artery took the place of the posterior collum branch

As in previous investigations, the vessels of the head of the femur were not visible in all the cases examined This might have been due to the small vessel diameter The lower limit for angiographic definition is generally assumed to be about 0.3 mm Great individual variations in the diameter and extension of the arteries exist, however Superimposition of the other vessels and a decrease in local concentration of the contrast medium in single cases may be a contributory factor

HIPP (1962) has described non filling, small diameter of the vessels and similar conditions as pathologic when present in fractures of the neck, necrosis of the femoral head, or in other affections of the hip However, this argument is refuted by the results of the present investigation This also revealed that atherosclerosis may involve the afferent vessels of the femoral head without causing disorder or skeletal changes in the hip The vascular findings, particularly the deviations from 'normal' described in this investigation, may naturally also be present in hips involved by fracture or necrosis The latter conditions are however, often accompanied by typical circulatory changes, as described in detail by MUSSBICHLER (1956, 1970)

### Conclusions

The results in general arteriography differed from those of semiselective arteriography in that the frequency of filling of the acetabular artery was higher in the former than in the latter Apart from this, there seemed to be no difference between both methods as regards filling of the femoral head vessels However, semiselective arteriography is superior in demonstrating the vascular anatomy of the hip because superimposition of the gluteal branches on the femoral head vessels is avoided

The anatomists' description of the vessels to the femoral head were basically confirmed However, deviations from the 'normal' anatomy were observed in 14 of 92 cases These concerned hypoplasia of the posterior collum branch (three cases) and anomalies of its origin (eleven cases) In two of the latter an ectopic origin was detected in the inferior gluteal artery The vessels of the head of the femur were not filled in all the cases Non filling may thus be part of the normal anatomy Selective internal iliac arteriography revealed the incidence of small anastomoses between the inferior gluteal artery and the posterior collum branch in three out of fifteen cases and the ectopic origin of a posterior collum branch in one case Selective internal iliac arteriography may thus be a useful complement to the other methods of arteriographic examination of the hip



The knowledge and recognition of the great variety of 'vascular findings' in the sound hip prevent them from being misinterpreted if incidentally present in affected hips

## SUMMARY

The vascular anatomy of the normal, unaffected hip was investigated by angiographic examinations in 92 cases. The examinations were carried out with a blunt Seldinger cannula, a straight polythene catheter or a loop-formed Ödman Ledin catheter inserted into the common femoral artery. The great individual variations in the vessels of the femoral head, the incidence of hypoplasia and anomalous origins of the posterior collum branch are emphasized.

## ZUSAMMENFASSUNG

Es wurde die Gefäßversorgung der normalen, nicht erkrankten Hüfte mittels Angiographie studiert. Es kamen dabei die stumpfe Seldinger Kanüle, ein gerader Polyethylen Katheter oder ein zu einem Loop geformter Ödman Ledin Katheter zur Verwendung. Die Untersuchung ergab u. a. beträchtliche individuelle Variationen der Femurgefäße sowie das Vorkommen von Hypoplasie und anomalem Ursprung des hinteren Collum Zweiges.

## RÉSUMÉ

L'anatomie vasculaire de la hanche normale saine a été étudiée par angiographie dans 92 cas. Les examens ont été pratiqués avec le trocart mousse de Seldinger, un cathéter rectiligne en polythène ou un cathéter incurvé de Ödman Ledin introduit dans l'artère femorale commune. L'auteur souligne la grande fréquence des variations individuelles des vaisseaux de la tête femorale, ainsi que l'existence d'une hypoplasie et d'une origine anormale de la branche postérieure de l'artère du col femoral dans plusieurs cas.

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## SUBMUCOSAL HAEMATOMA OF THE OESOPHAGUS DUE TO ANTICOAGULANT THERAPY

Report of a case

by

MICHAEL ADDRESS

In recent years, there have been many reports of haemorrhagic complications involving the intestinal tract due to the increasing use of anticoagulant drugs. These have included cases of intramural haematomas in the duodenum and in the jejunum, which have been demonstrated radiologically by survey films and barium examinations. CULVER *et coll* described a case of a jejunal haematoma and WIOT *et coll* two cases of duodenal haematomas complicating treatment with anticoagulants. These cases were diagnosed on barium examinations but SEARS *et coll* presented four cases of small bowel haematomas, three of which were diagnosable on survey films.

The small bowel is most often affected, particularly the duodeno jejunal junction region (ANSELL), but GABRIELE & CONTE described a case with haematoma of the sigmoid colon which developed during treatment with heparin, a narrowing of the lumen with oedematous folds was demonstrated by barium enema. The heparin treatment was discontinued and there was complete resolution of the lesion within three weeks.

GIROUX *et coll* reported a pharyngo-laryngeal haematoma induced by anti-coagulant therapy, and KIVIRANTA also described a laryngeal haematoma.

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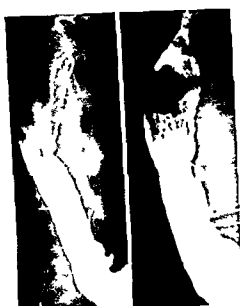


Fig 1



Fig 2

Fig 1 Large expansive process arising from the left postero-lateral wall of the oesophagus and protruding into the lumen which is slightly expanded. There is also a small hiatus hernia and oesophageal reflux.

Fig 2 Eight days later almost complete resolution of the lesion. There is still a slight infiltration of the posterior wall (between arrows).

occurring during such a course of treatment. Both patients developed severe respiratory obstruction.

WILLIAMS presented the case of a 77-year old woman (not on anticoagulants) who fell from her bed onto her outstretched hand and developed retrosternal pain. She had difficulty in swallowing and vomited a little blood. The pain and dysphagia eased over the following two days and on the third day after the fall a roentgen examination of the oesophagus was performed. An unusual, rather rhomboidal expansive process in the mid-oesophagus was found. The centre of the process was coated by barium with indefinite margins, constantly present. Oesophagoscopy was not undertaken as it was felt that this might be hazardous if the diagnosis of haematoma was correct. On the eleventh day after injury, a repeat barium examination revealed a return to normal appearances. This author discussed the possible mechanism and concluded that the lesion was more likely to be a submucosal haemorrhage, the tension leading to splitting of the overlying mucosa with subsequent haematemesis, rather than an incomplete form of oesophageal rupture involving only the mucosa and

submucosa. He considered that the reversion to normal appearance within only a few days was strongly in support of this diagnosis.

However, as far as the author is aware, no previous case of an oesophageal submucosal haematoma due to anticoagulant therapy has been reported.

### Case report

A diabetic woman aged 59 was started on anticoagulant therapy three months before admission when her mitral stenosis and incompetence with atrial fibrillation was found to be complicated by a non functioning right kidney. This was considered to be the result of an embolus and treatment with warfarin was commenced.

She was admitted following two episodes of haematemesis on the same morning. She also complained of a feeling of food sticking low in the oesophagus and pain in the right chest radiating to the right arm and right loin aggravated by eating. The anticoagulant therapy was immediately discontinued. On the day after admission an examination of the oesophagus was carried out. A large expansive process in the mid oesophagus was found (Fig. 1). This mass was arising from the left postero lateral wall of the oesophagus and protruded into the oesophageal lumen which was slightly expanded. A small hiatal hernia with oesophageal reflux was also demonstrated. On the next day she had a further haematemesis and on that day and the two following melaena motions were observed.

At oesophagoscopy four days after the examination a blue coloured soft mass was seen in the left postero lateral wall of the oesophagus 30 cm from the teeth.

The patient by a week after her admission was feeling much better and a roentgen examination nine days after admission and eight days after the initial barium examination showed an almost complete return to normal (Fig. 2) only slight irregularity of the wall being detectable at this examination.

### Discussion

This case is of interest in that an oesophageal haematoma complicating anti coagulant therapy does not appear to have been reported previously and the barium examination findings could be misinterpreted particularly if the fact that the patient is on anticoagulants is overlooked. The appearances were somewhat similar to, though more marked than, those described by WILLIAMS in his case of submucosal haemorrhage following remote trauma. In the present case the diagnosis is supported by the oesophagoscopy findings and as in the case reported by WILLIAMS, the rapid resolution of the lesion and the return to normal or almost normal appearance within a few days.

### Acknowledgements

The author wishes to thank Dr N. F. Jones for permission to publish this case report and Dr J. W. Pierce for his advice.

## SUMMARY

mucosal haematoma following remote trauma. The rapid resolution is a diagnostic feature of the lesion.

## ZUSAMMENFASSUNG

Submucöse Hamatome des Ösophagus infolge Therapie mit Antikoagulantia scheinen bislang nicht berichtet worden zu sein. Bei dem hier beschriebenen Fall ist das radiologische Bild dem bei einem beschriebenen Fall eines Submucosa-Hamatoms des Ösophagus nach einem entfernten Trauma ähnlich, aber starker ausgeprägt. Die rasche Auflösung ist ein diagnostisches Merkmal dieser Läsion.

## RÉSUMÉ

Il ne semble pas qu'on ait publié des cas d'hématome sous muqueux de l'œsophage dû au traitement anti-coagulant. Dans le cas présenté par l'auteur, les signes radiologiques étaient analogues à ceux qui ont été observés dans un cas publié d'hématome sous muqueux de l'œsophage après un traumatisme à distance, mais dans le cas présent, il était plus marqué. La rapide résolution des signes est un des caractères diagnostiques de cette lésion.

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## RETROPERITONEAL ABSCESS WITH GAS AFTER PERFORATION

by

LARS E. HENRIKSSON

Rupture of the alimentary canal into the retroperitoneal space is rare in comparison with perforation into the abdominal cavity. The appearances in conventional views are characteristic however. The rupture usually begins in the parts of the gastrointestinal tract that have no posterior peritoneal covering, in other words the dorsal wall of the stomach, the duodenum, and the ascending or descending colon.

From the etiologic aspect the traumatic forms, with laceration of the duodenum (MILLER 1916, COHN 1952, CLEVELAND & WADDELL 1963, RESNICOFF *et coll* 1967), predominate. Rupture of a duodenal ulcer with subsequent retroperitoneal emphysema has been described (PETREN 1916, SOMOGYI 1941, KOENIG & CULVER 1947), as has emphysema following perforation of a duodenal diverticulum (LUGINIAN 1950, SCHACKELTON 1963). Rupture of the colon may be due to malignancy or a diverticulum (CULVER & CONCANNON 1950). Retroperitoneal emphysema as a complication of enema has also been reported (BRUNTON 1960). Bacterial action on the contents of the perforation cavity may cause an abscess, the following three cases being illustrative of the latter. The condition is serious and usually accompanied by sepsis and shock.

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Fig 1 Case 1 Retroperitoneal abscess behind the stomach

### Case reports

*Case 1* Male aged 38, an alcoholic, was admitted with hematemesis and melena after suffering for two months from severe epigastric pain. A survey film of the abdomen revealed a retroperitoneal abscess with gas. On the following day the patient became unconscious following further melena. At operation a decimeter wide cavity containing pus and blood lay behind a large defect in the posterior wall of the stomach. The patient regained consciousness after the operation. He stated that for the previous six months he had been drinking relatively large amounts of alcohol daily while lying on his back. Repeat roentgenography of the stomach revealed regression of the abscess, three months later, a narrow, 2 cm long fistula from the dorsal part of the fornx was however still present.

*Case 2* Male aged 49, confessing to a large daily consumption of alcohol, was admitted with nausea and severe pain in the epigastrium. He was treated conservatively. The temperature rose gradually to about 39° C, and his general condition became affected. A fortnight after admission a survey film of the abdomen revealed gas lying retroperitoneally. Laparotomy was performed for probable abscess of the pancreas, and a cystic formation, about 25 cm in diameter, was evident behind the stomach and colon and was drained. Three months later, an attempt made to close the fistula disclosed a large branching cavity filled with a gelatinous mass behind the omental bursa. The site of the original perforation could not be established. The greater part of the pancreas was removed. The fistula from the right part of the cavity to the tail of the pancreas were in still open about 18 months later.

*Case 3* Woman aged 54 with a short history of biliary symptoms was examined by cholecystography and cholangiography. Concretions were observed in the choledochous duct. Cholecystectomy and choledochotomy were performed, but as only one stone was evident



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From the etiologic aspect the traumatic forms, with laceration of the duodenum (MILLER 1916, COHN 1952, CLFVELAND & WADDELL 1963, RESNICOFF *et coll* 1967), predominate. Rupture of a duodenal ulcer with subsequent retroperitoneal emphysema has been described (PETREN 1916, SOMOGYI 1941, KOENIG & CULVER 1947), as has emphysema following perforation of a duodenal diverticulum (LUCINIAN 1950, SCHACKELTON 1963). Rupture of the colon may be due to malignancy or a diverticulum (CULVER & CONCANNON 1950). Retroperitoneal emphysema as a complication of enema has also been reported (BRUNTON 1960). Bacterial action on the contents of the perforation cavity may cause an abscess, the following three cases being illustrative of the latter. The condition is serious and usually accompanied by sepsis and shock.

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### Discussion

Gaseous retroperitoneal abscesses have typical appearances in conventional films and consist of small gas-containing cysts within a relatively well delimited area. The appearances seem to be the same irrespective of the site from whence the perforation has originated and the type of bacteria in the abscess (Case 1 *S. aureus* and *A. aerogenes*; Case 2 *P. pyocyanea* and *E. coli*; Case 3 *S. aureus* and *E. coli*). According to FRIMAN-DAIL (1960), small gas cysts may occur in connection with acute pancreatic necrosis, but the present writer has come across no mention in the literature of necrosis of the pancreas with such a gaseous abscess as was observed in Case 2, in which perforation to the alimentary canal had probably occurred. The difference in the roentgen appearances between an abscess and acute perforation into the retroperitoneal space depends on the bacterial process. In acute rupture, the gas outlines the anatomic structures and follows the large blood vessels, in other words, in principle produces the same appearances as those obtained after retroperitoneal air insufflation for diagnostic purposes. A p. and lateral views will help to clarify the position and exclude the possibility of phenomena such as postoperative gas gangrene of the anterior wall of the stomach.

The perforation in Cases 1 and 2 was the result of chronic processes that had caused adhesion of the omental bursa, this was confirmed at operation.

Pneumatosis cystoides intestinalis, with its gas-containing cysts, may produce appearances similar to the cysts evident in retroperitoneal gas abscesses, especially if the pneumatosis is located in a colon flexure and the diaphragm. Investigations with contrast medium may often demonstrate that some of the cysts lie along the intestine. The individual cysts are furthermore often larger and of a smoother appearance.

### SUMMARY

A gas-containing retroperitoneal abscess arising after a perforation produces typical appearances in conventional films. Three cases are described. The difference in the signs between acute and chronic conditions is considered and discussed.

### ZUSAMMENFASSUNG

Retroperitoneale Gasabszesse nach Perforation haben typische Erscheinungen auf gewöhnlichen Röntgenfilmen. Drei Fälle werden beschrieben. Die Unterschiede bei akuten und chronischen Fällen werden diskutiert.

### RÉSUMÉ

Les abcès retro-peritonéaux contenant du gaz et apparaissant après une perforation donnent des images typiques sur les radiographies simples. L'auteur en décrit trois cas. Il étudie la différence des signes des abcès aigus et chroniques.



Fig 2 Case 2 Retroperitoneal abscess following perforation of a pancreatic cyst

duodenotomy was also undertaken. The operation was terminated after nearly 7 hours before all the concretions had been removed. Sepsis and refractory retention of the stomach contents developed postoperatively. A survey film of the abdomen obtained twenty days later disclosed a retroperitoneal abscess with gas within an area measuring  $20 \times 10$  cm and located behind the peritoneum lateral and dorsal to the duodenum. Further laparotomy established that the abscess was in communication with the duodenum through a faultily sutured section of the intestine. A fistula made after the second operation healed spontaneously. The patient was symptom free four and a half years after the operation.

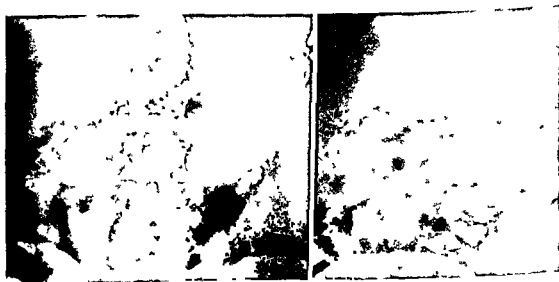


Fig 3 Case 3 Retroperitoneal abscess following faulty suturing of the duodenum

## ANATOMIC CAUSE FOR INTRAOSSICULAR CAVITIES IN TEMPORAL BONE TOMOGRAPHY

by

B SANDSTRÖM and H F WILBRAND

With modern tomographic techniques it is possible to demonstrate fine details of the temporal bone down to about the range of 0.3 mm and sometimes to reveal the presence of small cavities in otherwise intact and healthy ossicles. Such defects in the malleus and incus occur more often in young individuals but seldom in the middle aged or elderly. The authors have never observed these areas in chronic otitis but they have been noted in otosclerosis with an otherwise normal radiologic state.

Few reports of these areas occur in the literature. FREY et coll (1967) observed rarefactions in the ossicles of a patient examined by tomography for otosclerosis. KARLSSON et coll (1954), DAVIC et coll (1967) and GALIOTO & MARLEY (1963) performed micro- and macroradiographic as well as micro-pneumographic investigations of isolated ossicles without obtaining any explanation concerning the anatomic basis for the defects in the ossicles sometimes found at temporal bone tomography.

The authors wished to determine the precise nature of these appearances by

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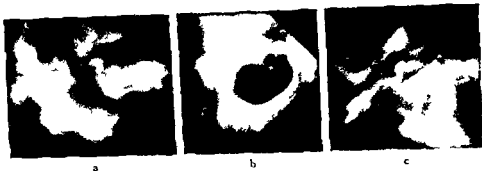


Fig 2 Middle ear tomograms of an adult male with small cavities in the head of the malleus and body of the incus a) Ap with 15—20° lateral inclination (Guillen Vignaud), b) lateral and c) Stenvers views

1) A thin intermediate linear decalcification in the tomograms of the stapedial crura could not be definitely identified as a defect. The size of the crura of the stapes lies at the limit of tomographic resolution.

The tomograms in the male revealed small areas similar to cavities in the head and the body of the malleus and incus (Fig 2), although these were less well defined and extensive than in the child. The translucent spaces were surrounded by a thick cortical layer and the continuity of a cavity throughout an ossicle, clearly visible in the child, was absent.

Photography of the decalcified translucent ossicles demonstrated cavities corresponding to the tomographic appearances. The infantile ossicles consisted of shells of compact bone surrounding large central cavities, clearly revealed by their blood contents. The cavities in the ossicles of the adult were smaller, star-shaped and confined to the malleolar head and the body of the incus (Fig 3).

Microscopy demonstrated that the ossicles of the infant had large central cavities with smooth inner walls, surrounded by lamellar bone with small clusters of hyaline cartilage. The cavities were filled by a loose mesh of reticular cells with many osteoblasts and ordinary erythrocytes. The appearances were those of progressing ossification by internal apposition of bone (Figs 3 and 4). The changes in the adult were somewhat different. The cavities were smaller and star-shaped and surrounded by thicker walls of lamellar bone with occasional small islets of hyaline cartilage, the cavities were filled by a loose network of mesenchymal cells surrounding central, tortuous vessels with radiating branches (Fig 5). No inflammatory reaction or destructive processes were observed. There was no evidence of the bone marrow structures typically present in ordinary skeletal bone.

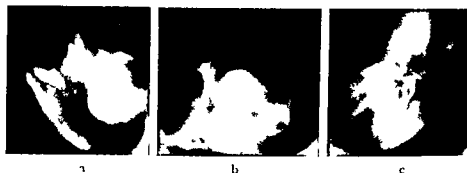


Fig. 1. Middle ear tomograms of a 6 day old baby girl. Defects are present throughout the malleus and incus. a) Ap with 15–20° lateral inclination (Guillen Vignaud), b) lateral and c) Stenvers views.

direct comparison between the tomograms and the anatomic and histologic findings in cases in which ossicles with small cavities occurred.

**Material and Methods.** Tomography of a series of temporal bone specimens from human cadavers was carried out with a Massiot-Philips Polytome and hypocycloid movement. Focal spot size 0.3 mm and enlargement factor 1.3, 55 to 70 kV, and 50 to 64 mA with an exposure time of 11.6 sec (double hypocycloid movement). Structurix D7 (Agfa Gevaert) exposed in the seriograph with six exposures on one 24 × 30 cm film without intensifying screens, the cassette was lined with leadfoil. Electromechanical dodging was used to diminish the density range. The specimens were mounted to simulate positions obtained in clinical tomography.

The films of a baby girl and of an adult male were selected as presenting the characteristic defects. The baby had died at 6 days of congenital heart disease without any signs of temporal bone malformations. The malleus and incus were removed and fixed in 4% buffered formaldehyde for three days followed by decalcification in 5% EDTA for three weeks, dehydration in graded alcohols and clearing in xylene. At this stage the ossicles were translucent and photography against a light background showed up the intraosseous cavities well.

The specimens were then embedded in paraffin and serially sectioned. The sections were mounted on glass slides and treated with hematoxylin-eosin or Giemsa stains.

### Results

The ossicles in the tomograms of the child were of a delicate structure with clearcut cortical lining of the malleus and the incus with cavities throughout the body and crura as well as of the head and manubrium of the malleus (Fig

### Discussion

The investigation appears to indicate that tomographically demonstrated defects in the ossicles consist of vascular cavities of a size depending on age and maturity.

The ossicles of the middle ear are derivatives of the branchial arch system. Despite their common origin the development of the stapes differs at an early stage from that of the malleus and incus and is more closely linked with that of the otic capsule (ANSON & BAST 1959). Its substructure matures before the malleus and incus, which being substitution bone, pass through a morphogenic course of different stages in development (ANSON *et coll.* 1962). The corresponding branchial arteries disappear early in development and are replaced by a form of vascularization that is unique and unlike any other type observed in skeletal bone (NAGER & NAGER 1953, HAMBERGER *et coll.* 1963). The malleus and incus are thus vascularized by small branches of the anterior tympanic artery. They enter as nutrient arteries and communicate with an extensive network of mucosal branches that penetrate the bone wall irregularly throughout the whole extent of each ossicle (See especially Fig. 3d, indicating the vascular distribution inside the ossicles).

Large 'marrow cavities' occurred in the infantile ossicles. During childhood and adolescence diminution of these cavities by internal bone apposition changes the radiologic appearances. The cavities become smaller and lie mainly in the head of the malleus and the body of the incus. The defects may thus be considered to represent a normal anatomic variant rather than osseous disease, e.g. otospongiosis.

Otospongoid tissue in the active stage of otosclerosis appears as decalcified areas in temporal bone structures and are apparent provided they be of sufficient size to be resolved tomographically. Otosclerosis is mainly confined to the otic capsule and changes seldom occur in the malleus and incus, judging by the small number of cases reported in the vast literature (COWELL 1940, ENGSTROM 1940, KELEMEN 1939, NAGER 1944, NYLEN 1949, SLEECKS *et coll.* 1967). Since otosclerosis of the malleus and incus is rare, defects in the ossicles should be regarded as normal anatomic variants probably even in cases of manifest otosclerosis in structures deriving from the otic capsule. The vascular cavities evident in the present material obviously do not represent the most common type of internal ossicular architecture, since other authors (NAGER & NAGER 1953, ANSON & BAST 1959, ANSON *et coll.* 1964) describe a spongoid network of anastomosing vascular channels as typical of the internal ossicular structure of the malleus and incus of the adult. Cavities are accordingly apparent only occasionally in middle ear tomograms of adults and are not a regular finding. The





Fig. 3. Ossicles from a six day old baby gull (a, b and c) and incus from an adult male (d). The configuration of the dark areas corresponds to the cavities in the tomograms (a) and (c). Photographs of decalcified malleus and incus before sectioning (b) and (d). Section through the centre of the malleolar head showing the central vascular cavity (d). Photograph of decalcified incus with asteroid arborization of the central vascular cavity.



Fig. 4. Section through the centre of the head of the malleus from a six day old baby gull. The intraosseous cavity is filled with a loose mesh of mesenchymal tissue.



Fig. 5. Corresponding section from an adult male. A smoothly outlined cavity containing tortuous vessels surrounded by a loose mesh of mesenchymal cells.

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incidence of this anomaly would appear to require further investigations in a larger, more representative series. Such investigations are in progress and preliminary histologic evidence suggests that roentgenologically visible vascular cavities may be expected to occur in about 15 per cent of cases. A full account will be given elsewhere (SANDSTROM 1970).

## SUMMARY

The anatomic basis of central defects in the ossicles of the middle ear observed at tomography has been investigated by comparative roentgenologic and anatomic examinations. Such areas would appear to be due to a normal variant of intra ossicular vascularization rather than to bone disease.

## ZUSAMMENFASSUNG

Eine vergleichende rontgenologische und anatomische Untersuchung wurde vorgenommen um die Ursache von zentralen Defekten in den Gehörknöchelchen die bei Tomographie beobachtet werden zu ergründen. Solche Defekte scheinen eher von einer normalen Variante der Gefäßversorgung als von einer Knochenkrankheit bedingt zu sein.

## RÉSUMÉ

Les auteurs ont étudié par des examens radiographiques et anatomiques comparés la nature anatomique des lacunes centrales observées en tomographie dans les osselets de l'oreille moyenne. Ces lacunes paraissent dues à une variation normale de la vascularisation intra ossiculaire plutôt qu'à une affection osseuse.

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## ENCEPHALOGRAPHY IN THE DIAGNOSIS OF CONVEXITY BLOCK HYDROCEPHALUS

by

TORGVN GREITZ and ARNE GREPE

Communicating hydrocephalus is caused by obstructive processes in the intracranial cerebrospinal fluid pathways outside the ventricular system. The obstruction is said to be most often located at or close to the level of the tentorial incisura. This so-called incisural block is produced by inflammatory processes such as meningitis (MESSERT & BÄFR 1966, FEINBERG & LAUGER 1965, LEHRER et coll 1967) and spontaneous or posttraumatic subarachnoid haemorrhage (FOLTZ & WARD 1956, CRONQVIST 1967). Its cause in children may be perinatal intracranial haemorrhage (GRANHOJN & RÅDBERG 1963). The diagnosis of incisural block is usually based on encephalographic evidence of failure of air to pass the level of the tentorial notch except in small quantities. Several reports, usually based on small materials, recorded that in patients with the syndrome of 'low pressure hydrocephalus' dilated subarachnoid channels above the tentorial incisura may be filled at encephalography and produce appearances resembling those of cerebral atrophy (LEHRER 1968, GREITZ et coll 1969, EKBOM et coll 1969, GREITZ 1969, OJEMAN et coll 1969). No mention is made, however, as to the frequency of this latter type of finding in relation to that of incisural block.

Table

*Summary of clinical data from 23 patients with hydrocephalus*

| Cause of hydrocephalus              | Number of patients | Clinical improvement |        |        |
|-------------------------------------|--------------------|----------------------|--------|--------|
|                                     |                    | Absent               | Slight | Marked |
| Trauma                              | 7                  | 4                    | 1      | 2      |
| Subarachnoid haemorrhage            | 2                  | —                    | 2      | —      |
| Ectasia of basilar artery           | 7                  | 2                    | 1      | 4      |
| Saccular aneurysm of basilar artery | 1                  | —                    | 1      | —      |
| Sinus thrombosis                    | 1                  | —                    | 1      | —      |
| Unknown                             | 5                  | 2                    | 2      | 1      |

It would not appear unusual for air to pass in fairly large quantities above the tentorial incisura in patients with clinical signs and symptoms of low pressure hydrocephalus. As some of these patients benefit from a shunting procedure it was considered valuable to analyse the encephalographic findings and to correlate them with the results of operation in an attempt to establish criteria for the selection of patients suitable for such procedures.

**Material and Methods** All patients operated upon during the years 1967, 1968 and the first half of 1969, because of signs and symptoms of low pressure hydrocephalus were included. Clinical data were not available in 3 patients, who were therefore omitted from the investigation, there then remained 23 patients, 7 females, 16 males, ranging in age from 21 to 73, with a mean of 49 years. The hydrocephalus was due to trauma in 7 patients, to subarachnoid haemorrhage in 2, to ectasia of the basilar artery in 7, to aneurysm in 1 and to sinus thrombosis in 1 patient. The etiology was unknown in 5 patients (cf. the Table).

Encephalography was performed mainly by the technique of LINDGREN (1951). Great care was taken to ensure filling of the basal cisterns and the sulci over the convexity. The encephalographic criteria of hydrocephalus were dilated lateral ventricles and absence of air over the convexities. The hydrocephalic index (LINDGREN) was determined as the quotient between the greatest width of the anterior horns and the maximum internal skull width.

The width of the third ventricles was measured both anteriorly and posteriorly, and the greatest value was related to maximum internal skull width (cf. BORGERSEN 1966). The height of the fourth ventricles was measured by the method of AMUNDSEN & GRIMSRUD (1966) as the perpendicular distance between the floor of the fourth ventricle and the fastigium. Because the fourth ventricle dilates during the encephalographic procedure (OBERSON *et coll.* 1969) this

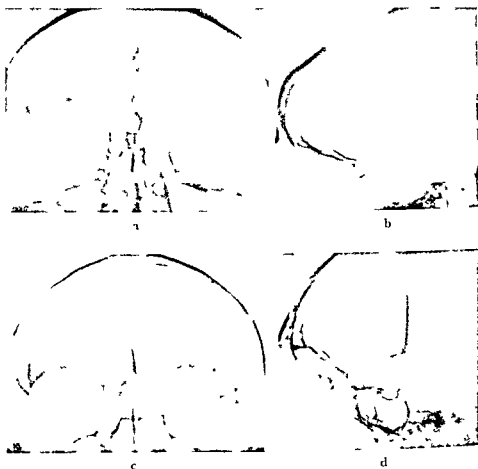


Fig 1 Cisternographic changes in low pressure hydrocephalus a) and b) Incisural block, no air passes beyond the dilated pontine and interpeduncular cisterns, marked dilatation of the temporal horn c) and d) Convexity block, hydrocephalus with air supratentorially in the interhemispheric and Sylvian fissures, no air over the convexity, dilatation of the temporal horn

latter measurement was taken from the first roentgenogram obtained. SJAASTAD et coll (1969) reported dilatation of the temporal horn to be a frequent finding in pressure hydrocephalus. The present authors were, however, not able to find any single measurement that well correlated to the size of the temporal horn, due to the slight inconstancy of the projections used in the material. No actual measurements were therefore taken and the dilatation of the temporal horn was evaluated by mere inspection and classified as absent, slight or marked.

RIHSA cisternography by the DI CUIRO method was carried out in 14 patients and demonstrated a slow but otherwise normal circulation in 3, incisural block in 4 and a convexity block, i.e. filling of the interhemispheric and Sylvian fissures, but no absorption maximum over the convexity, in the remaining patients. Filling

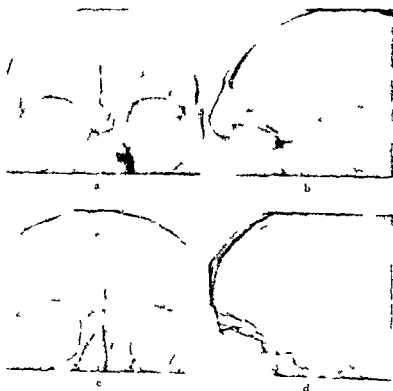


Fig 2 Encephalographic changes in low pressure hydrocephalus a) and b) Convexity block hydrocephalus following sinus thrombosis with air in the marked area c)

of the lateral ventricles occurred in 9 patients who presented all the above mentioned types of CSF circulation. In conjunction with RIHSA cisternography the lumbar CSF pressure was measured with an open-end manometer in 14 patients and was always below 18 cm. In 3 of these and in 5 additional patients the intraventricular pressure was measured during operation and did not exceed 16 cm of water.

The clinical signs and symptoms were evaluated immediately before and during the week after the operation and in addition three to five weeks later. The patients had usually been seen by the neurosurgeon who performed the shunting procedure; those with ectasia had also been examined by a neurologist and the



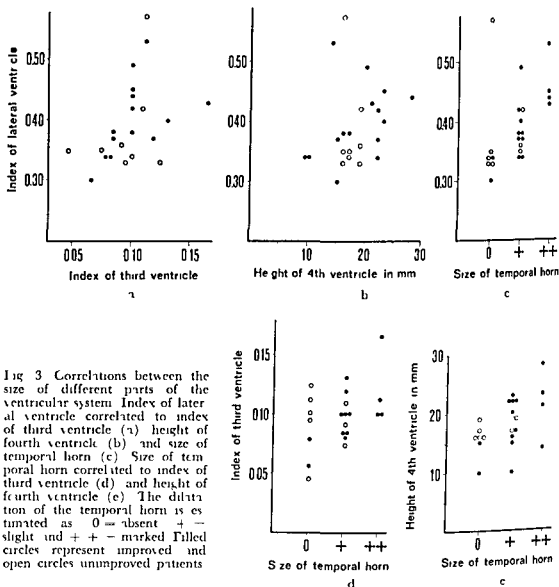


Fig 3 Correlations between the size of different parts of the ventricular system. Index of lateral ventricle correlated to index of third ventricle (a) height of fourth ventricle (b) and size of temporal horn (c). Size of temporal horn correlated to index of third ventricle (d) and height of fourth ventricle (e). The dilatation of the temporal horn is estimated as 0 = absent + = slight and ++ = marked. Filled circles represent improved and open circles unimproved patients.

findings are published elsewhere (Larsson et coll.) The patient's condition before and after the operation was considered as regards each sign and symptom and these were then synthesized in an overall judgement in order to obtain a general idea of the patient's improvement, which was classified as absent, slight or marked. This classification was made without knowledge of the encephalographic findings.

## Results

Air passed the basal cisterns and appeared supratentorially in the Sylvian and interhemispheric fissures in all but 4 of the 23 patients of the present series. The

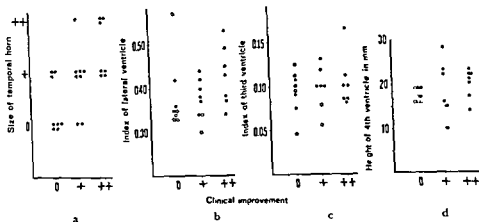


Fig 4 Clinical improvement (graded as 0 = absent + = slight and ++ = marked) correlated to size of temporal horn (a) index of lateral ventricle (b), index of third ventricle (c), and height of fourth ventricle (d). The clinical improvement appears to be most closely related to the size of the temporal horn. Open circles represent patients without dilatation of the temporal horn.

air was arrested infratentorially in the basal cisterns in 2 of these patients and did not pass beyond the suprasellar cisterns in the other 2 patients. Three of these 4 patients were clinically improved by operation. Two patients, who were originally evaluated as having no air over the convexities, were found at a re-evaluation to have a small amount of air over the convexity in the frontal and occipital but not in the parietal areas, these 2 patients did not improve. The supratentorially located air lay mainly in the interhemispheric and in Sylvian fissures which were frequently dilated (Figs 1 and 2). Only the interhemispheric fissure was sometimes filled and in other instances unilateral filling of the Sylvian fissure was evident. No correlation between the supratentorial distribution of the air and the operative results was recorded. The width of the lateral ventricles as expressed by the LINDGREN index varied from 0.30 to 0.57. This index was not well correlated to that of the third ventricle or to the height of the fourth ventricle (Fig 3a and b). The size of the temporal horn was only vaguely correlated to the size of the fourth and third ventricles or to the degree of dilatation of the remainder of the lateral ventricle (Fig 3c, d and e). The last two correlations seemed, however, to improve when only patients who benefited from the operation were considered. The appearance of the indentation of the caudate nucleus into the lateral ventricles could be estimated in 21 patients and varied, being convex in most and concave in a few patients, usually with marked dilatation of the ventricle (Fig 4). Out of the 23 patients, 15 were improved following the operation, 7 of them showing marked improvement. No improvement

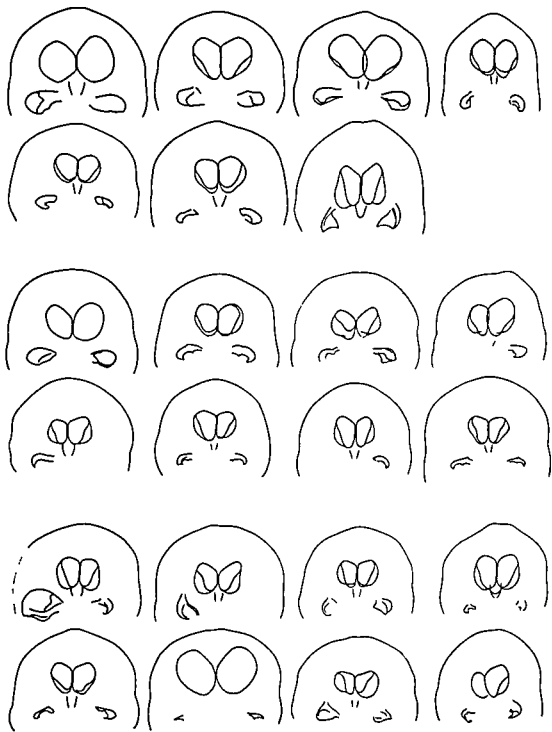


Fig 5 Anterior part of the ventricular system in 23 patients with communicating hydrocephalus treated with ventriculostomy. *Upper group* includes patients with marked improvement. All patients in this group had dilated temporal horns. *Middle group* represents patients with slight improvement. *Lower group* includes patients with no improvement. Only 3 patients were considered to have dilated temporal horns. Upper left patient in this group had been operated for a subdural haematoma and a laceration of the right temporal lobe.

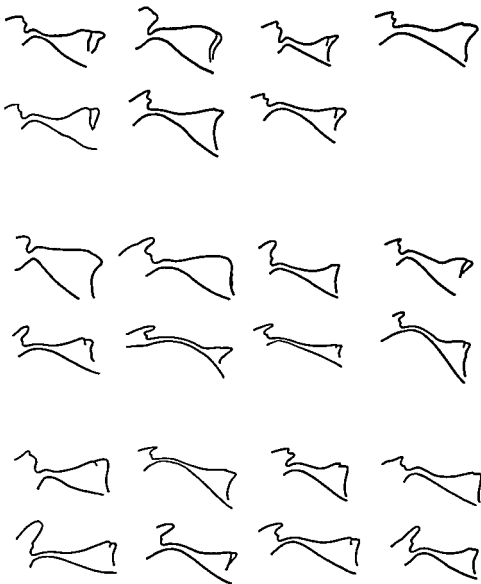


Fig 6 Same groups of patients as in fig 5. An everted anterior medullary velum is present in 3 instances and only in improved patients.

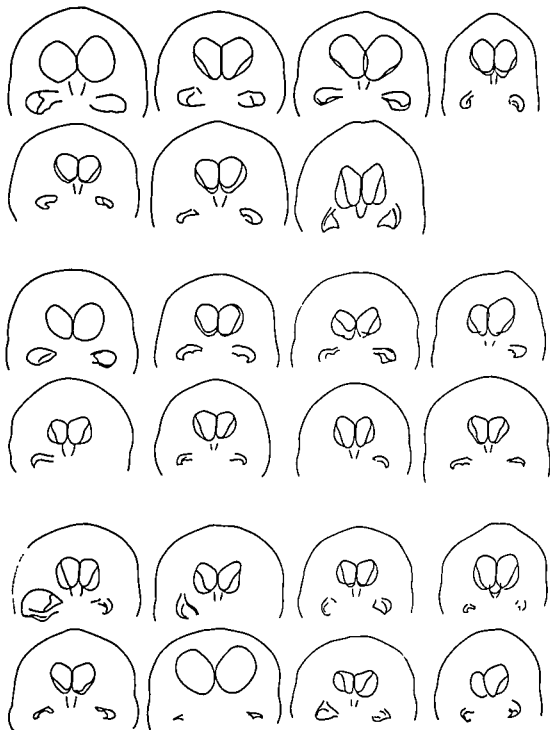


Fig 5 Anterior part of the ventricular system in 23 patients with communicating hydrocephalus treated with ventriculo-atrial shunting. *Upper group* includes patients with marked improvement. All patients have dilated temporal horns. *Middle group* represents patients with slight improvement. Ventricular dilatation is less marked than in the upper group. *Lower group* includes patients without clinical improvement following operation. Only 3 patients were considered to have dilated temporal horns. Upper left patient in this group had been operated for a subdural haematoma and a laceration of the right temporal lobe.

frequent finding in pressure hydrocephalus and mentioned two cases of probable normal pressure hydrocephalus with this finding. No attempts to correlate these observations with the results of operation were made. The present investigation indicates that in order to select patients suitable for operation an evaluation of the width of the temporal horn seems to be as important as any other method.

The dilatation of the ventricular system depends on two factors: the intraventricular pressure, or rather the ventricular subarachnoid space pressure gradient, and the tensile strength of the wall of the ventricles, i.e. that of the brain tissue (GESCHWIND 1968). The latter factor is likely to be affected in the degenerative diseases. This does, however, not occur, at least not primarily, in hydrocephalus where pressure changes are the initial cause of the dilatation. This may explain why the appearances vary in these two conditions and would at the same time form the basis for the difference in the results of shunting procedures.

### Conclusion

Obstructions of the cerebrospinal fluid pathways may be situated adjacent to the pachyonian bodies and produce a slight and sometimes marked dilatation of the pathways in the Sylvian and interhemispheric fissures with compression of the cerebral hemispheres against the calvaria, this results in the typical encephalographic appearances for convexity block hydrocephalus. Because it is the most frequent finding in low pressure hydrocephalus, its true nature should be recognized and not confused with cerebral atrophy. The operation results indicate that those patients having dilated temporal horns are more liable to benefit from surgery than those in whom the horns are normal.

### Acknowledgement

This investigation was supported by a grant from the Medical Research Council of the Swedish Life Offices.

### SUMMARY

The encephalographic appearances in a material of 23 patients with low pressure hydrocephalus have mostly been considered as being due to convexity block hydrocephalus. The features of this condition are described and the importance of the width of the temporal horn in the selection of patients suitable for operation is emphasized.

### ZUSAMMENFASSUNG

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was noted in 8 patients. No marked correlation between the clinical improvement and the size of the lateral ventricles, as expressed by the LINDGREN index or to the third ventricular index or to the height of the fourth ventricle, was observed (Fig 4b, c and d). However, with regard to the degree of dilatation of the temporal horn it was quite obvious that patients who improved mostly had wider temporal horns than those who failed to improve (Figs 4 and 5). All but 3 of the 16 patients who were considered to have dilated temporal horns improved from the shunting procedure, and out of 7 patients without such dilatation only two showed slight improvement. Definite flattening or reversal of the indentation of the caudate nucleus was noted only in 5 patients who all improved (Fig 5). Obvious flattening or reversal of the anterior medullary velum occurred only in 3 patients all with clinical improvement (Fig 6).

### Discussion

Incisural block has been considered to be the most frequent finding in communicating hydrocephalus at least following intracranial haemorrhage such as subarachnoid bleeding (CROQVIST 1967) or perinatal haemorrhage (GRANHOLM & RÅDBERG 1963). Four of the patients of the present material had this block at cencephalography and 3 of these improved after operation. In view of the fact that 12 of the patients with air filling of the interhemispheric and Sylvian fissures improved, it is reasonable to assume that these patients were suffering from low pressure hydrocephalus. Hence, it appears as though these cencephalographic signs are more common in the syndrome of low pressure hydrocephalus than is incisural block. The dilated interhemispheric and Sylvian fissures represent the widened cerebrospinal fluid pathways, these pathways are filled both at cencephalography and RIHSA cisternography. The dilatation of the lateral ventricle causes compression of the brain which may be responsible for the absence of filling over the convexity. The main site of obstruction is probably close to the pecthionian bodies and in one of the patients a sinus thrombosis had been diagnosed earlier by angiography. These cencephalographic appearances of dilated CSF pathways and absence of air filling over the convexity are probably therefore diagnostic of 'convexity block hydrocephalus'. It would appear that a pathologic CSF circulation is always revealed at RIHSA cisternography in this condition although judging from the present material RIHSA cisternography alone does not seem to be sufficient as a criterion for the selection of patients suitable for operation. Two of the 3 patients who had a slow CSF circulation without definite block did not improve. Two out of 7 patients with convexity block and 2 out of 4 patients with incisural block did not benefit from the operation. Three out of 9 patients with filling of the ventricular system were unimproved.

SJAASTAD et coll (1969) considered dilatation of the temporal horn to be a

frequent finding in pressure hydrocephalus and mentioned two cases of probable normal pressure hydrocephalus with this finding. No attempts to correlate these observations with the results of operation were made. The present investigation indicates that in order to select patients suitable for operation an evaluation of the width of the temporal horn seems to be as important as any other method.

The dilatation of the ventricular system depends on two factors: the intraventricular pressure, or rather the ventricular subarachnoid space pressure gradient, and the tensile strength of the wall of the ventricles, i.e. that of the brain tissue (Gerschwind 1968). The latter factor is likely to be affected in the degenerative diseases. This does, however, not occur, at least not primarily, in hydrocephalus where pressure changes are the initial cause of the dilatation. This may explain why the appearances vary in these two conditions and would at the same time form the basis for the difference in the results of shunting procedures.

### Conclusion

Obstructions of the cerebrospinal fluid pathways may be situated adjacent to the pial bodies and produce a slight and sometimes marked dilatation of the pathways in the Sylvian and interhemispheric fissures with compression of the cerebral hemispheres against the calvaria, this results in the typical encephalographic appearances for convexity block hydrocephalus. Because it is the most frequent finding in low pressure hydrocephalus, its true nature should be recognized and not confused with cerebral atrophy. The operation results indicate that those patients having dilated temporal horns are more liable to benefit from surgery than those in whom the horns are normal.

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### ZUSAMMENFASSUNG

Encephalogramm

Druckwerte

Patienten

Die encephalographischen Erscheinungen dieser Krankheit werden beschrieben und die Bedeutung der Weite des Temporalhornes bei der Auswahl von Patienten, die sich zur Operation eignen, wird betont.



## RÉSUMÉ

Les images encéphalographiques sur une série de 23 malades atteints d'hydrocéphalie à basse pression sont considérées dans la plupart des cas comme dues à une hydrocéphalie par blocage à convexité. Les auteurs décrivent les caractéristiques de cette affection et soulignent l'importance de la largeur de la corne temporale pour choisir les malades justiciables d'une opération.

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## LUMBAR MYELOGRAPHY WITH WATER-SOLUBLE CONTRAST MEDIUM IN CHILDREN

by

RASMUS STENSTROM and MARGARETA LINDFORS

Both gas and three types of positive contrast media only contrast media such as Pantopaque, emulsions like SH 617 L, and water-soluble contrast media, e.g. Abrodil and Conray, Meglumin 282 have been used in lumbar myelography (ARNELL 1948, ZEITLER & DIETZ 1965, AHLGREN 1969). Lumbar myelography has been performed in children under general anaesthesia with gas or Pantopaque (INGRAHAM & MATSON 1954, JACKSON & THOMPSON 1959, GRISPERDT 1963, STRAND 1969), no separate reports seem however to have been published on the employment of water soluble contrast media. The youngest patient in the series of EDGREN et coll (1966) comprising 1000 myelographies was for example 14 years old. An age of less than 14 was regarded by PANTER (1955) as a contraindication to use of Abrodil in lumbar myelography.

Gas myelography causes slight side effects (ZEITLER & DIETZ). LINDGREN & TORNELL (1969) wrote as follows: 'Gas is in many respects more satisfactory as a contrast medium than the positive contrast media'.  
the positive

Table 1

*Lumbar myelographies with water-soluble contrast medium in the 17 children of the present series classified according to age and indication*

| Indication              | Age      |           |           | Total |
|-------------------------|----------|-----------|-----------|-------|
|                         | <5 years | <10 years | <15 years |       |
| Possible tumour         | 2        |           | 1         | 3     |
| Micturition disturbance | 1        | 2         |           | 3     |
| Sciatica                |          |           | 11        | 11    |
| Total                   | 3        | 2         | 12        | 17    |

however less suitable for the investigation of root sleeves and for demonstrating angiomas'

Only contrast media have produced slight side effects during the course of the investigation, but more severe sequelae may occur later, e.g. arachnitis, foreign body granuloma and fat embolism (ZEITLER & DIETZ). The following statements were made by FISCHER (1965) following experimental investigations in cats: 'Following Pantopaque myelography the cats showed uniform evidence histologically of acute and chronic meningeal irritation' and 'SH 617 L produced a faint contrast and caused severe meningitis in the animals, indicating a significant toxic hazard in its clinical use'. LINDGREN & TORNELL, who tried SH 617 L in the dog, stated 'The results in these animals as well as the complications mentioned in the literature have caused us to refrain from carrying out clinical trials with this preparation'.

FUNKQUIST (1961) and FUNKQUIST & OBEL (1961) tested the water soluble contrast medium Abrodil (Kontrast U, Leo) in experimental studies in dogs. It caused the same signs as other hypertonic saline solutions, viz. oedematous and necrotic foci in the spinal medullary tissue. The extent of the changes increased with the strength of the solution. The phenomenon was especially conspicuous in the range 15 to 20% and over. The side effects also increased with fall in blood pressure, which led to delayed resorption of the contrast medium. The experiments with Abrodil performed by O'MALLEY (1965) gave deviating results but 'however, in spite of a thorough search, with the reports of FUNKQUIST & OBEL in mind, no oedematous foci or other intramedullary lesions of any kind could be detected'. ZEITLER & DIETZ stated that myelography with water-soluble contrast medium was best performed under general anaesthesia, because central nervous irritation with fall in blood pressure, collapse and spasms were then avoided. AMUNDSEN et coll (1963) and EDGREN et coll

Table 2

*Pathologic lumbar myelographies with water soluble contrast medium in children*

| Age (years) | Sex | Clinical diagnosis   | Myelographic diagnosis   |
|-------------|-----|----------------------|--------------------------|
| 3           | F   | Dermoid cyst         | Intraspinal tumour       |
| 11          | M   | Lumbosacral syndrome | Disc protrusion at L4-5  |
| 12          | M   | Lumbosacral syndrome | Disc herniation at L5-S1 |
| 13          | M   | Lumbago              | Disc protrusion at L3-4  |
| 13          | F   | Ischiatic syndrome   | Disc herniation at L4-5  |
| 14          | M   | Nephroblastoma       | Intraspinal tumour       |
| 14          | F   | Lumbago              | Disc protrusion at L4-5  |
| 14          | F   | Ischiatic neuritis   | Disc herniation at L4-5  |

reported no serious complications, and HIRSCH et coll (1969) stated 'More serious complications have also been reported but these have probably been due mainly to an inappropriate technique'. After scanning the literature AHLGREN & PRAESTHOLM (1969) concluded that late changes following Abrodil myelography have been described only in a few investigations. FISCHER, who injected Conray into the subarachnoid space in cats, observed no histologic evidence of toxicity. Conray Meglumine 282 has been employed in lumbar myelography without spinal anaesthesia (AHLGREN).

*Material and Method* The series consists of 17 children, 9 of whom were boys and 8 girls, treated during the period 1959-1969. General anaesthesia was used in 15 patients, once in combination with spinal anaesthesia, only spinal anaesthesia was employed in 2 patients (Xylocain 5 %). The inclination of the examination table was 15 to 20° with the patient's head raised. Contrast medium of the Abrodil type (Kontrast U 20 %, Leo) was used in 16 patients. The dosage was 0.2 to 0.3 ml/kg body weight. A dosage of 0.3 ml was never exceeded (FURUKUJI & OBEL). The relatively new medium Conray Meglumine 282 was employed in 1 patient in 1969. Conray Meglumine 282 was diluted with 25 % cerebrospinal fluid before injection (AHLGREN), in the only patient in our series thus investigated the undiluted dose was 0.1 ml/kg body weight. The dosage of the two types of contrast medium corresponded to 20 to 30 mg I/kg body weight. Injection was performed slowly over 15 to 30 seconds so that the medium was more effectively diluted with cerebrospinal fluid. When Kontrast U was used, the examination was performed with a horizontal beam direction but with Conray Meglumine 282, both injection and radiography were performed with a vertical beam direction and during television fluoroscopy.



Fig 1



Fig 2

Fig 1 Girl aged 3 operated on for sacral dermoid cyst one year previously. Contrast column interrupted at the level of L2—3, indicating an intraspinal tumour. A dermoid cyst was histologically diagnosed.

Fig 2 Boy aged 14 operated on for nephroblastoma one year previously. Pelvic metastases were observed and myelography disclosed a defect in the contrast column at the level of L5 suggesting an intraspinal tumour.

(AHIGREN) Following the examination the patient was kept for six hours semi-upright with the upper part of the body at an angle of 70°.

### Result

The age distribution of the series appears in Table 1. The youngest patient was 20 months of age and the oldest was 14 years. Table 1 also gives the indications for myelography. The possibility of an intraspinal tumour was confirmed in 2 out of 3 patients. Three patients had disturbances of micturition although myelography was normal. Eleven patients aged 11 to 14 years were investigated on account of sciatica. Disc herniation was diagnosed in 3 of these, aged 12, 13 and 14 years respectively, and the diagnosis was confirmed at operation. In another three patients, aged 11, 13 and 14 years, disc protrusion was diagnosed, these were treated conservatively. The positive myelographic findings appear in Table 2.



Fig 3 Girl aged 14 with pain radiating down the right leg. Myelography suggested disc herniation with prominence of the disc and broadening of the root pocket at the level of L4—5 (arrow) confirmed at operation.

*Side effects* No fall in blood pressure occurred when the examination was performed under general anaesthesia. However, in the three examinations under spinal anaesthesia, the blood pressure fell 20 to 25 mm during the first hours after the examination. Immediately after the examination 3 of the patients developed light muscle spasms in the calf for a period of 10 to 15 minutes. Headache with or without backache occurred in 8 patients for one to two days following the myelography although 5 of these patients had these symptoms before the examination. A raised temperature, leukocytosis or elevation of the ESR after myelography was not encountered.

### Conclusions

Many authors (INGRAHAM & MATSON, JACKSON & THOMPSON, GRYSPEERDT) have recommended Pantopaque for myelography in children. However, it seems ill advised to expose young patients to the risk of severe late complications such as may be connected with the use of both oily and emulsified contrast media. In general gas myelography appears to be preferable in children, but a water soluble contrast medium seems to be more useful in lumbar myelography which requires adequate filling of the root pockets.

As emphasized by HIRSCH et coll, the severe complications caused by myelography with water soluble contrast medium seem to be due to an inap-



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As emphasized by HIRSCH *et coll*, the severe complications caused by myelography with water soluble contrast medium seem to be due to an inap-



propriate technique. Myelography in children is best performed with water-soluble contrast medium under general anaesthesia. Complications due to fall in blood pressure are thus less likely to occur, and in addition the examination is generally safer.

## SUMMARY

Lumbar myelography with water-soluble contrast media was performed in 17 children, the youngest of which was 20 months old. A fall in blood pressure was avoided by employing general anaesthesia. It is suggested that the young should not be exposed to the risk of late complications connected with the use of oily contrast media.

## ZUSAMMENFASSUNG

Lumbale Myelographie mit wasserlöslichen Kontrastmitteln wurde an 17 Kindern vorgenommen, das jüngste Kind war 20 Monate alt. Die Allgemeinnarkose verhinderte einen Abfall des Blutdruckes. Demgemäss scheint es unratsam, Kinder den Spätfolgen öliger Kontrastmitteln auszusetzen.

## RÉSUMÉ

Les auteurs ont fait une myelographie lombaire avec moyen de contraste hydrosoluble chez 7 enfants dont le plus jeune était âgé de 20 mois. Ils ont évité une baisse de la tension artérielle en utilisant l'anesthésie générale. Ils pensent que les enfants ne devraient pas être exposés au risque de complications tardives dues au moyen de contraste huileux.

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## CENTRIPETAL DESCENDING PHLEBOGRAPHY IN AXILLARY VEIN THROMBOSIS

by

Ulf BERGMALL

Deep venous thrombosis of the upper limb and its central draining veins is comparatively rare. It may be a consequence of tumours or other pathologic conditions of the upper thoracic region, or of central venous catheterisation, in which event the nature of the primary lesion decides the prognosis. The so called idiopathic axillary vein thrombosis is the most common, and has a favourable prognosis — disabling sequelae, analogous to the consequences of central venous thrombosis of the lower limb seldom occur.

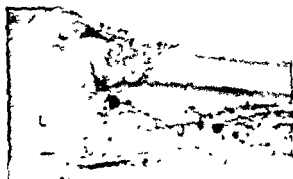
As to the technique of phlebography in this region, various recommendations are encountered in the literature. LINDBLOM (1946) used a lateral recumbent, centripetal descending technique for examination of the mediastinal veins. The axillary vein appeared to be well filled by contrast medium though the report deals only with the mediastinal pathology.

LINDBLOM (1952) advocated a lateral recumbent, centripetal ascending technique, similar to the one for the lower limb recommended by GREITZ (1954). For examination of the mediastinal veins LINDBLOM referred to LINDBLOM.

FISCHER (1951) used an angiocardigraphic technique with the patient in the supine horizontal position. GVOZDANOVIC & OBERHOFER (1953) with the same technique injected both arms rapidly and simultaneously for the examination of

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a) Supine horizontal position. The main venous trunks are incompletely filled with contrast medium; central collaterals are seen.



b) Centripetal ascending phlebography. Only the wide cephalic vein and the central collaterals are contrast filled.



c) Centripetal descending phlebography. Floating thrombi are outlined in the main veins.

Fig. 1. Case 1.

the upper mediastinal veins and inflows. They pointed out that unilateral contrast injection in the supine position may produce a false impression of thrombosis by the inflow of blood without contrast medium from non injected regions. They also stated that 'roentgenologically it is almost impossible to differentiate between obstruction produced by inflammatory changes, idiopathic thrombosis and infiltration by tumours'.

a) Supine horizontal position. In direct signs of axillary vein occlusion with central collaterals



b) Centripetal ascending phlebography. Essentially the same information as in (a)



c) Centripetal descending phlebography. A slightly narrow central segment of the axillary vein not filled in (a) or (b) now appears (arrows)



Fig 2 Case 2

WELLAUFER (1957) recommended a serial angiographic technique in the supine horizontal position with a high pressure injector. In later textbook editions, as in recent reports (GULLMO 1964, EILERS 1965, MAY & NISSEL 1965, WERNITSCH et coll 1969, JACOBSSON & SCHLOSSMAN 1969), the same posture seems to be favoured, though positioning of the patient is not usually discussed.

BERGVALI (to be published) has pointed out that during centripetal ascending phlebography of the lower limb in the semi erect position, distribution of the contrast medium is dependent mainly on haemodynamic factors as the medium



Fig 3 Normal case Upper  
are adequately demonstrated  
from other regions Lower  
collapsed and devoid of con

uu      (c) s i s i o w i m p e d m e n t

which is injected peripherally follows the blood stream. Should there be marked or complete flow impediment in a deep vein the affected venous segment will be bypassed and remain unfilled, a part of the vein peripheral to the block may not fill. The length of the block may be determined by the length of the stream to stream.

capacity.      (c) s i s i o w i m p e d m e n t  
indirect signs of flow impediment without valid information regarding the exact position or the nature of the block.

These circumstances may be elucidated by the author's method of centripetal descending phlebography by which the heavy contrast medium is directed with the help of gravity towards the interrupted venous segment. The impeding lesion

will thus be directly delineated. This principle has been shown to be valid in acute deep venous thrombosis of the lower limb. It may also be useful in examination of the upper limb region, which is illustrated by the two following case reports. Contrast medium (Urografin 45 %), 40 to 60 ml in each position, was administered by rapid manual injection through a standard disposable teflon cannula, inner diameter 0.7 mm.

### Case reports

*Case 1* Man, aged 49, with clinical signs of acute left axillary vein thrombosis of some six days duration.

At initial phlebography in the supine horizontal position (Fig. 1a) incompletely filled main venous trunks and central collaterals were seen. A short segment of the subscapular vein almost filled by a thrombus was not a conclusive finding.

Centripetal ascending phlebography with the patient in the lateral recumbent position and the arm vertically downwards (Fig. 1b) revealed that the wide cephalic vein was the only visible outflow from the arm. The main trunks were not filled.

Centripetal descending phlebography in the lateral recumbent position and the arm vertically upwards (Fig. 1c) indicated the true nature of the occlusion. The cephalic vein appeared narrow and the collaterals were filled. The contrast medium by force of gravity also filled the central parts of the occluded trunks and the occlusions were depicted as floating thrombi.

*Case 2* Woman, aged 28, had had acute right axillary vein thrombosis about a year previously. Phlebography on recurrence of symptoms had been performed and revealed signs of an occlusion of the right axillary vein.

The present phlebography was carried out because of slight swelling of the arm. The examination in the supine horizontal position (Fig. 2a) produced indirect signs of axillary vein occlusion as at the previous examination performed in the same position.

Centripetal ascending phlebography yielded a similar amount of information (Fig. 2b) though the veins close to the expected occlusion appeared to be somewhat better filled.

At centripetal descending phlebography the actual site of the occlusion was demonstrated (Fig. 2c) as another 5 cm of the main trunk proximal to the main collateral were contrast filled. This slightly narrowed segment represented the part of the vein which though patent was bypassed; it was therefore not filled until the contrast medium was directed centrally by gravitation.

Centripetal ascending and descending phlebography findings from a case without clinical or roentgenologic signs of venous flow impediment are presented for comparison (Fig. 3). As is to be expected, the ascending phlebography adequately demonstrated the main venous trunks of the arm and the axillary region while the contrast medium in the subclavian vein was diluted by the inflow of blood without medium from other regions. At descending phlebography the veins were not very well demonstrated, despite rapid injection of the contrast medium, due to the fact that there was no central flow impediment.

### Conclusions

The distribution of contrast medium at phlebography is directed by blood flow and force of gravity. These two factors may operate in the same direction or counteract each other. By positioning of the patient, the force of gravity may be utilized to direct the contrast medium to regions with otherwise no apparent flow. Parts of the venous system not demonstrable by centripetal ascending phlebography in cases of central occlusion or severe flow impediment may thus be adequately depicted by centripetal descending phlebography. Indirect diagnostic signs are then replaced by the direct demonstration of the lesion.

### SUMMARY

The importance of considering gravity as well as haemodynamic factors during phlebography is illustrated by two cases of axillary vein thrombosis.

### ZUSAMMENFASSUNG

Der Wert, die Gravität sowie andere hamodynamische Faktoren während Phlebographie zu berücksichtigen, wird mit zwei Fällen von Thrombose der Vena axillaris illustriert.

### RÉSUMÉ

L'auteur donne deux exemples de cas de thrombose de la veine axillaire montrant qu'il est important de tenir compte de la gravité et des facteurs hemodynamiques aux cours de la phlebographie.

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## ANGIOGRAPHIC DIAGNOSIS OF SPLENIC LESIONS FOLLOWING BLUNT ABDOMINAL TRAUMA

by

J LEPASOON and T OLIN

The first splenectomy for trauma is believed to have been performed by a French surgeon in 1581. A text of 1876 referred to 26 splenectomies from the world literature during the period 1549–1869, 17 of which were carried out for traumatic lesions (TERRY et coll 1936). Since the first 'modern' operation of this kind by RIEGNER in 1892, however, an extensive literature on the subject has accumulated, especially during recent years. Most of these lesions are caused by blunt traumas and splenic rupture is one of the more common subcutaneous abdominal injuries, occurring in 15 to 48 % of cases (reviews by CLOUTIER & ZAEFFEL 1958, McCORT 1966, PROSCIA & SORISIO 1968, TERRY et coll 1936). Kicks by horses had been the classical mode of injury but by 1926 ruptures caused by motor traffic had come to the fore (QUEVU 1926). Traffic, sport and industrial accidents account for an increasing frequency of the lesions.

Although vast experience has been gained by now and operation mortality had been reduced from 46 % in 1900 (TERRY et coll) to practically nil in 1958 (PARSONS & THOMPSON 1958) splenic rupture still carries a substantial mortality, amounting to about 20 % in some recent larger series (e.g.

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Fig 1 Case 33 Extravasation and intrasplenic haematoma causing parenchymal defects and displacement of arterial branches Shunting with early filling of the splenic vein Evidence of extrasplenic haematoma a) Selective angiogram of the celiac axis b) Specimen

also appear as free fluid in the peritoneal cavity and, if in the gastrosplenic ligament, may reach the wall of the stomach and deform and cause serration of the greater curvature Rib fractures are present in about a tenth of the cases (except in children, whose thoracic cage is more elastic (SCHWARTZ et coll 1959, UPADHYAYA & SIMPSON 1968)) and fluid is sometimes present in the left pleural cavity It is recognized that these signs are relatively inconstant and not pathognomonic The spleen can ordinarily not always be outlined and, conversely, even the presence of a well defined spleen of normal size in survey films does not rule out the possibility of splenic injury

Various procedures involving different contrast media have been employed in attempts to improve the diagnostic possibilities BURKE & MADIGAN (1933) used an accumulation of Thorotrast in the reticulo-endothelial system to demonstrate a splenic rupture previously verified at operation Examinations in the prone or the Trendelenburg position after a barium meal have been proposed as a means of demonstrating displacement or serration of the stomach (BANCROFT 1943, SCHORR & DANON 1967) The production of a pneumoperitoneum has also been advocated (BIRSNER et coll 1953, MCCORT 1966, PORCHER et coll

SARGISON et coll 1968) This is partly due to the serious associated injuries that occur with fairly constant frequency as well as to the diagnostic difficulties often encountered

*Delayed haemorrhage* The diagnosis may be fairly easy in the typical case with a history of trauma, shock and left upper quadrant abdominal pain with rigidity and dullness as well as pain in the left shoulder (Kehr's sign) Symptoms and signs may be missing or vague and laboratory findings (anemia, elevated white cell count) inconsistent in other cases This is more likely to occur when the primary bleeding is intrasplenic or subcapsular or when a capsular tear is temporarily closed by clotting or adhesions to the omentum or viscera A fresh episode of bleeding with acute manifestations may then occur, the so called delayed rupture or more correctly 'hemorragie en deux temps', the French term (BELL & STEFFIE 1944) The first trauma may be slight and sometimes even overlooked, the second bleeding is often initiated by further slight trauma or a rise in intra-abdominal pressure Small physiologic contractions of the spleen may be a contributory factor (DORSON 1950) The symptom-free period between these two events was recognized as early as 1863 by CHANDEL (cited by VIVIANI 1956), later it was called 'the latent period of Baudet' after a French physician who stressed its importance in 1907 McILROY (1932) described the syndrome in detail and introduced an arbitrarily chosen minimum interval of 48 hours between the trauma and second bleeding as a prerequisite for the designation 'delayed haemorrhage' Extensive reviews have been presented by ZABINSKI & HARKINS (1943) of 177 cases, and recently, in 1966, by SIZER et coll of 312 cases According to the former authors cases of this kind constitute 14% of all splenic ruptures, in other materials higher proportions of up to 35% occur (AAKIHUS & ENGEL 1967) The latent period is under a week in 50% of the cases, while 25% of the secondary bleedings take place during the second week The longest known interval is 2 1/2 years (JOHNSON 1954)

A correct diagnosis was originally made in only 20% of cases in the large series reviewed by SIZER et coll As the mortality without operation has been 77 to 100% (ZABINSKI & HARKINS) it is naturally essential that diagnostic accuracy be improved Spontaneous healing occurs but infrequently, although in rare instances it may take place even after serious injuries, such as hilar tear (ARMITAGE 1929) or avulsion of the spleen into separate fragments (URADIMAYA & SIMPSON 1968) A haematoma sometimes slowly becomes a traumatic cyst

*Roentgen diagnostics* Roentgen survey films may provide signs of splenic rupture Haemorrhage may cause displacement of adjacent structures, i.e. the left side of the diaphragm upwards, the splenic flexure of the colon (with sometimes the left kidney) downwards and the stomach medially Blood may



Fig 3 Case 8 Examples of large intrasplenic haematomas causing parenchymal defects and displacement of arterial branches extra splenic haematoma

cases of false negative diagnoses were recorded. The examinations were performed on liberal indications, i.e. whenever uncertainty regarding the diagnosis existed. However, during the same period a number of splenectomies were performed without angiography where the diagnosis of splenic rupture was evident on clinical grounds and could be confirmed by survey abdominal films.

The angiographies of the 35 cases with splenic rupture are summarized in the table in chronologic order. A few of the cases have been reported elsewhere. The age distribution is typical with a relative preponderance of younger males. As regards aetiology 14 of the lesions were caused by traffic accidents (car or motorcycle, and in one case a go-cart), in 12 other cases falls were responsible. Three patients were kicked by horses, 2 were injured playing football and 2 children were hit in the abdomen by the handle of their bicycle. A definite

Table (cont.)

| Case number  | Age (years) | Sex | Interval between trauma and angiography | Site of injection | Spasm of splenic artery | Displaced intra splenic vessels | Parenchymal defects | Extravasation | Extra splenic bleeding | Early venous filling |
|--|-------------|-----|---|-------------------|-------------------------|---------------------------------|---------------------|---------------|------------------------|----------------------|
| 33   | 48          | M   | <1 day                                  | Celiac artery     | +                       | +                               | +                   | +             | +                      | +                    |
| 34   | 44          | F   | <1 day                                  | Celiac artery     | +                       | +                               | +                   | +             | +                      | —                    |
| 35   | 44          | M   | 1 day                                   | Celiac artery     | —                       | +                               | +                   | +             | +                      | +                    |
| Total positive findings                            |             |     |   |                   | 12                      | 32                              | 38                  | 32            | 21                     | 15                   |
| Including cases 12, 21 and 30 (not operated upon)  |             |     |   |                   | 11                      | 30                              | 33                  | 29            | 20                     | 14                   |
| Percentage (35 examinations, 32 operated patients) |             |     |   |                   | 31 %                    | 86 %                            | 94 %                | 86 %          | 57 %                   | 40 %                 |

Most of the authors preferred a selective angiographic technique (cf Fig 1). There is good correlation between the findings of different observers and the angiographic signs of splenic rupture are now well known, displacement of intrasplenic vessels, defects in the filling of the parenchyma and extravasation of contrast medium are common findings, whereas arteriovenous shunting less often occurs. The spleen sometimes appears to be displaced by an extrasplenic haematoma. On the whole the findings are in accordance with the results of experimental work carried out in dogs (SCHREIBER et coll 1968). This work also confirmed the clinical rule (JOHNSON 1954) that for a given trauma the type and severity of the lesion cannot be predicted.

Angiography has now been used at this centre for the last decade in abdominal trauma. A possible lesion is examined with selective angiography of the celiac axis with superselective catheterization of the splenic artery, if feasible. Only serious technical difficulties indicate aortography. When there is marked stenosis of the celiac axis, injection into the superior mesenteric artery usually provides useful information (Fig 2). A red Ödman-Ledin catheter with two side-holes is usually inserted into the artery by the Seldinger technique. About 30 to 40 ml Urografin 60 to 76 % or Isopaque Coronar are injected for each film series in adults, with an injection flow rate of 10 ml/sec. Two or three projections are used in each case, the right posterior oblique position providing valuable information on the spleen.

Correct angiographic diagnosis of splenic injury was made in 35 cases while splenic lesions could be excluded in 65 cases in a total material of 104 cases during the past decade. False positive diagnoses were made in 4 cases. No



Fig 5 Case 34 Gross displacement of ruptured spleen by extrasplenic haematoma.



Fig 6 Case 13 Large extravasations (in addition to other signs of rupture)

technically unsatisfactory, in one case there was disagreement about interpretation of the angiograms and in another case evaluation was difficult due to displacement of the spleen through a ruptured diaphragm. The diagnoses could not be confirmed by retrospective evaluation of the angiograms. Parenchymal defects also occur in other pathologic states, such as infarcts and infiltration of the spleen. However, when combined with displacement of intrasplenic vessels the defects may well outline a haematoma (Fig 3).

Care must be taken not to misinterpret lobation of the spleen, the organ may be divided by a deep cleft (Fig 4) but the edges are smooth and rounded. Displacement of vessels occurred with the same frequency as extravasation of contrast medium. The latter actually seems to be the most typical and reliable sign and may occur in several forms: most commonly there is a diffuse leakage into the parenchyma, giving it a mottled appearance (Figs 1 and 5). This mottling is coarse and irregular and as a rule confined to one part of the spleen. It must be differentiated from the more even mottling sometimes occurring in normal cases (cf. AAKHUS & ENGE 1967) and probably caused by filling of the sinusoids. In other instances aneurysm-like extravasates or large pools of contrast medium are encountered (Fig 6).

A phenomenon that has not received much attention in the literature is



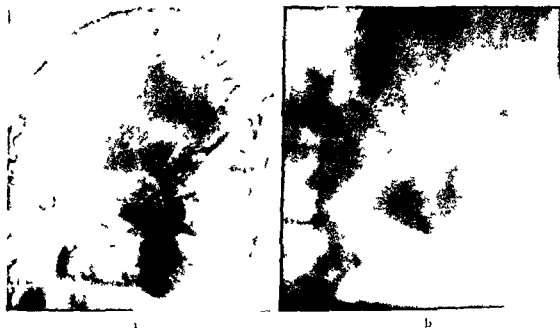


Fig. 1. Examples of lobation (a) and accessory spleen (b) at lower pole. Unlike ruptures the indentations have well defined smooth margins.

history of trauma could not be obtained in 2 cases. The clinical signs in all these patients were inconclusive. Laboratory procedures were of limited value: some degree of anaemia was present in 17 of the cases and a raised white cell count in 17 cases.

*Conventional roentgenography.* The spleen could be outlined in survey films in 12 cases and in 6 of these it appeared enlarged from the beginning. In 2 cases the spleen had increased in size when the examination was repeated while in a third instance it lost its distinct outline. The left side of the diaphragm was raised in 2 cases and ruptured in 1 case, in 4 cases there was fluid in the left pleural cavity. Fifteen cases had rib fractures and 12 had fractures in other parts of the body. Some influence on the splenic flexure was evident in 12 cases, in one case there was an impression upon the left kidney. Definite serration of the outline of the greater curvature of the stomach was present only in 4 cases and signs of fluid in the abdomen in 2 cases.

*Angiography.* The most common signs of injury in this series were defects in the parenchyma. These are, however, sometimes difficult to evaluate and the authors feel that they should not be relied upon as sole evidence of splenic rupture. The above-mentioned four false positive diagnoses were all based on this sign alone without other typical findings. Two of these examinations were



Fig 8 Case 30 a) Four days after trauma and 3 days following operative repair of left side of diaphragm. Multiple extravasations and central parenchymal defects (Contrast medium in the stomach) b) Fourteen days later The extravasations have disappeared

angiographic changes originally evident in these three cases could not be differentiated from those of other cases. They were, however, not of the most marked type.

An expectant policy was likewise adopted in Case 24 because of the paucity of abdominal symptoms. The second angiography indicated that the original extravasation had disappeared but parenchymal defects and displacement of vessels persisted. Intrasplenic and subcapsular haematomas were evident at operation.

In Case 16 clinical signs soon disappeared but a control angiography disclosed definite progress of the signs of injury. A third angiographic study started a fortnight later but was not completed because of a reaction to the contrast medium. The patient was operated upon and the presence of a traumatic lesion of spleen confirmed.

The last patient in this group (Case 28) underwent operation at another hospital two days after a go-cart accident. A rupture of the liver was sutured, the spleen was considered normal. The patient was then referred to our centre and celiac axis angiography performed on the day following operation. This indicated in addition to the liver injury, extensive extravasation in the spleen. A week later, after a rise in the leukocyte count, the patient developed signs of further intra abdominal bleeding. Repeat angiography demonstrated intra and extrasplenic haematomas and were confirmed at operation (Fig 10). This case illustrated the development of a classical 'delayed haemorrhage' and it is



Fig 7 Case 29 Lesion of an arterial branch with arteriovenous shunting

spasm of the splenic artery. It occurred in about a third of the cases (cf Fig 9). Arteriovenous shunting usually manifests itself by early filling of the splenic vein (Figs 1, 2, 6), a larger arteriovenous communication may sometimes be evident (Fig 7). Displacement caused by an extrasplenic haematoma will be discussed later.

*Findings at repeat angiographic examinations.* The signs described may represent reversible changes. The angiographic examination was repeated in 6 cases (Table). Case 30 was operated for a rupture of the left side of the diaphragm. The displaced viscera were replaced in the abdomen and the rupture closed by suture. The spleen was examined by inspection and palpation and considered to be normal. Yet angiography three days later revealed definite signs of splenic injury, which had almost vanished a fortnight later, thus indicated that healing had taken place (Fig 8). Two other cases had multiple bone fractures that required special orthopaedic care, as the abdominal symptoms rapidly resolved no laparotomy was performed. Control angiographies failed to present the previous signs of splenic injury (Fig 9). The

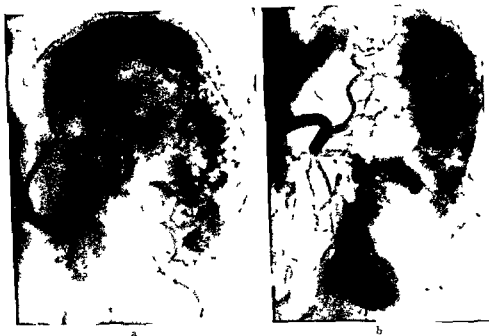


Fig 10 Case 28 a) 3 days after accident Ap projection Multiple extravasations with small parenchymal defects b) One week later following clinical signs of further bleeding Right posterior oblique projection The central extravasate is larger and a haematoma has appeared in the lower lateral part of the spleen The distance between the lower pole of the spleen and the thoracic wall has increased

liver injuries, in one case a lesion of the left kidney was apparent in the aortogram and in another case a corresponding lesion was demonstrated by a nephroangiography performed during the same examination

*Clinical results* One patient suffering from multiple injuries including contusion of the liver, cerebral concussion, etc., died postoperatively. Another patient, who also had multiple fractures and skull injuries developed meningitis one week after splenectomy but recovered. The rest of the patients made on the whole uneventful recoveries but 4 of them have later been operated for intraperitoneal adhesions.

The 3 patients with spontaneously healed splenic lesion have been controlled and have had no abdominal symptoms or signs whatsoever.

### Conclusions

Angiography permits good evaluation of splenic injuries and provides a means of ruling out what has been called occult i.e. not diagnosed, rupture of

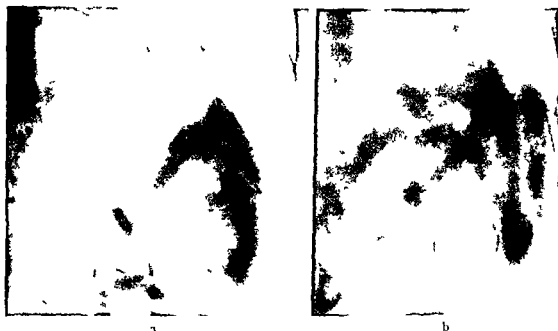


Fig. 9. Case 12. a) One day after injury. Spasm of splenic artery. Intrasplenic haematomas and mottling due to extravasation. Evidence of extrasplenic haematoma. b) 34 days later. Normal calibre and course of splenic artery. No extravasation with only a small filling defect in the upper pole of spleen. The extrasplenic haematoma has disappeared.

especially noteworthy that no injury of the spleen was detected at the first surgical exploration.

*Findings at operation.* Splenectomy was performed in 32 cases, i.e. in all those except the 3 with signs of healing referred to above, in all of them the diagnosis of splenic rupture was confirmed at operation. Appreciable quantities of blood were present in the abdominal cavity in 24 cases. In one of them signs of fluid were present in the survey films and in 19 cases evidence of extrasplenic haematoma had been noted at angiography. None of these signs was found in the remaining 4 cases. In one case in which extrasplenic bleeding had been suggested at angiography, no blood was present in the abdomen. Of course, some bleeding may have occurred after the examination in the 4 cases but these findings indicate that only really gross displacement of the spleen (Fig. 5) may be interpreted as due to a haematoma outside it. The position of the spleen normally varies considerably (KREEL & MINDEL 1969).

Further confirmation of the diagnosis was obtained by pathologic examination in 28 of the 32 cases. The spleens removed were otherwise normal except in one case in which some signs of infection were evident at microscopy.

*Additional angiographic findings.* The angiographic procedure permitted the diagnosis of associated lesions as well. Information in 4 cases was obtained on

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the spleen. At present it is the only method that can directly demonstrate the extent and character of the lesion. It has not provided the means of predicting the prognosis in the individual case but repeat examinations offer a possibility of following eventual healing. Further experience in this field is much needed.

A correct angiographic diagnosis of splenic rupture was made in 35 cases over the last decade. The main signs of injury were parenchymal defects (94% of lesions confirmed at surgery) in combination with displacement of intrasplenic vessels (86%) as well as extravasation of contrast medium (86%). Spasm of the splenic artery (31%) and arteriovenous shunting (40%) were less commonly noted. Displacement of the entire spleen may be caused by an extrasplenic hematoma (57%) but should be judged with due regard to normal variations in position. Repeat examination in two cases indicated progress and in one case partial regress of the signs of injury. Splenectomy was performed in 32 cases. Clinically spontaneous recovery and healing could be demonstrated by repeated angiography in 3 cases.

## SUMMARY

A correct angiographic diagnosis of rupture of the spleen was made during the last decade in 35 cases while in the remaining 69 cases of the material splenic lesions could be excluded. The characteristic appearances are described and attention is directed to the operation findings and subsequent histories.

## ZUSAMMENFASSUNG

Mittels Angiographie war es möglich im vergangenen Jahrzehnt eine Milzruptur in 35 Fällen korrekt zu diagnostizieren und in 69 Fällen eine solche auszuschliessen. Die charakteristischen Röntgenzeichen, die operativen Befunde und der weitere klinische Verlauf dieser Fälle werden besprochen.

## RÉSUMÉ

Au cours des dix dernières années les auteurs ont fait un diagnostic angiographique exact de rupture de la rate dans 35 cas et ont pu éliminer des lésions spléniques dans les 69 autres cas de cette série. Ils décrivent les aspects caractéristiques et attirent l'attention sur les constatations opératoires et sur l'évolution ultérieure.

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Table 1

*Contrast media and equimolar sodium chloride solutions*

| Contrast medium   | Sodium chloride solution |
|-------------------|--------------------------|
| Urografin 30 %    | 2.56 %                   |
| Urografin 45 %    | 4.09 %                   |
| Urografin 60 %    | 5.59 %                   |
| Urografin 76 %    | 7.67 %                   |
| Bilgrafin forte   | 2.07 %                   |
| Periodal H        | 3.82 %                   |
| Periodal U        | 4.30 %                   |
| Isopaque 260      | 4.24 %                   |
| Isopaque Cerebral | 4.51 %                   |
| Isopaque 350      | 5.99 %                   |
| Isopaque Coronar  | 6.50 %                   |

sodium metrizoate solution, with an iodine concentration of 260 mg/ml, was determined in 4 cases. In all other cases the experiments were carried out with the commercially used so-called balanced Isopaque preparations.

Hamsters weighing about 100 g were anaesthetized with Nembutal 30 mg/kg i.m. The cheek pouch was everted and exposed over a glass plate so that a proper condensor system could be used for transillumination (Fig. 1). The body temperature was maintained and the cheek pouch was irrigated with Tyrode's solution at constant temperature (37° C) during the experimental procedure to obtain a standardized local environment, the circulation in the cheek pouch being extremely sensitive to dehydration and change in temperature. All pouches that



Fig. 1 Bird's eye view of exposed cheek pouch of hamster

## CHANGES IN VASCULAR PERMEABILITY AFTER LOCAL APPLICATION OF ROENTGEN CONTRAST MEDIA IN THE HAMSTER CHEEK POUCH

by

S E SORESEN

BRÄNEMARK et coll (1969) reported that all contrast media currently in use cause microcirculatory disturbances to a varying degree to the hamster's cheek pouch after their local application. Signs of damage to the endothelium were demonstrated by an increasing number of white cells adhering to the vessel wall and sometimes thrombus formation. The present investigation was therefore undertaken to find out whether these microcirculatory changes may be associated with an increase in vascular permeability. As all contrast media are hypertonic solutions special consideration was given to the possible relation between the osmolarity of the media and changes in the vascular permeability. The significance of the hypertonicity of the contrast media was also analysed in simultaneously performed vital microscopy investigations.

*Material and Methods* The contrast media and equimolar chloride solutions investigated appear in Table 1. The change in permeability caused by a pure

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Table 2

*Contrast media number of deposits and sodium chloride solutions*

| Contrast medium   | Number of deposits | Sodium chloride solution |
|-------------------|--------------------|--------------------------|
| Urografin 11.2 %  | 8                  | 5*                       |
| Urografin 30 %    | 12                 | 7                        |
| Urografin 45 %    | 9                  | 6                        |
| Urografin 60 %    | 7                  | 5                        |
| Urografin 76 %    | 5                  | 2                        |
| Biligradin forte  | 5                  | 3                        |
| Periodal H        | 7                  | 3                        |
| Periodal U        | 5                  | 2                        |
| Isopaque 260      | 9                  | 4                        |
| Isopaque Cerebral | 7                  | 2                        |
| Isopaque 350      | 7                  | 4                        |
| Isopaque Coronar  | 5                  | 3                        |
| Isopaque 260**    | 4                  | 2                        |
| Total             | 90                 | 48                       |

\* According to information a 11.2 % Urografin solution is isotonic  
 The experiments with the corresponding salt solutions were therefore performed with Tyrode's solution

\*\* Pure sodium metrizoate solution with an iodine content of 260 mg/ml

housing, focussing bellows, and Leitz Elmar 1:4.5/135 mm lens. The distance between focus and films was 250 mm. After the Kodachrome II daylight colour film had been processed the light absorption was measured by means of a light densitometer in the areas where the contrast media had been deposited as well as in the surrounding cheek pouch regions. Light from a fixed source passed through a condenser system and after this through the specimen. Some of the light is absorbed as it traverses the film, the rest being conducted through the lens system of a microscope (Leitz obj. Pl. 4X, NA 0.1 — projector 4X Zeiss Jena) and into a photoelectric tube adapted to the eyepiece. A photocell in the tube transformed the light into an electric current whose strength depended on the intensity of the invading light. The strength of the current was measured by a microammeter.

Ten different measurements were made with this equipment in each deposit area and 10 in the adjacent tissue regions. The difference in average light absorption between the deposit area and surrounding region was considered to be a representative measure of staining intensity and thereby of increase in capillary

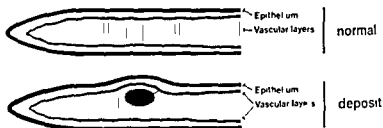


Fig 2 Diagrammatic representation of the experimental procedure. The normal exposed cheek pouch and site of application into the tissue

exhibited abnormal microvascular topography and function within 15 minutes after exposure were rejected

A standardized dose of contrast medium or hypertonic sodium chloride solution (0.05 ml) was deposited with a fine hypodermic needle in the upper layer of the everted cheek pouch (Fig 2). This technique ensures that the substance penetrates the pouch tissue and establishes intimate contact with the vessel wall, perivascular tissue and tissue fluid. Three different deposits were made in each pouch, the distance between each site of injection being approximately 10 mm. In comparing the toxic effect on the microcirculation and the change in vascular permeability the contrast medium and the equimolar sodium chloride solution, these solutions were always injected in the same pouch (Table 2). The velocities and rheology of the corpuscular and plasma flow, the intravascular shape and behaviour of the blood cells, and the structure of the vascular wall and perivascular cells in the deposit area and the adjacent pouch tissue were analysed in vital microscopy investigations. The changes in vascular permeability were studied by analysing the leakage of protein-bound dye.

Fifteen minutes following the deposition of the contrast medium or salt solution in the cheek pouch, 1.5 ml Evan's blue (vital dye T-1824, Mol. wt. 960.83) were injected intravenously into one of the hamsters hind legs, after such an injection the dye becomes attached to the circulating plasma albumin and forms a stable dye-protein complex (RAWSON 1943). If the contrast medium or salt solution deposited earlier in the cheek pouch has interfered with the function of the microvascular wall, and thereby increased the permeability of the microvessels, the protein-bound dye leaks from the vessels and the deposit area gradually becomes stained. The intensity of this staining was measured as follows.

The cheek pouch was photographed by a standardized procedure before and immediately after the application of the test substance. Films were then taken 20, 40, 60, 90, 120, 240 and in some cases 300 minutes after the injection of Evan's blue. The photographic equipment consisted of a Leica body with reflex

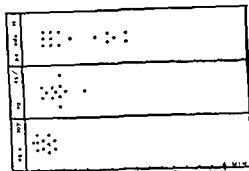


Fig 3 Diagrammatic representation of time interval between application of contrast medium into the tissue and restitution of microvascular flow velocities. Closed circles indicate contrast medium and open circles equimolar sodium chloride solutions

The lowest concentration of Urografin (mixture of sodium and methylglucamine salt of diatrizoic acid in the proportion 1:6:6) just able to cause momentary circulatory standstill in a selected small venule was estimated in a number of experiments to be in the range 70 mg iodine/ml to 75 mg iodine/ml, corresponding to a solution of about 15%. Corresponding iodine concentrations were found diluting the commercial preparations Isopaque 260 (sodium salt of metrizoic acid with addition of small amounts of  $\text{Ca}^{++}$  and  $\text{Mg}^{++}$ ) and Isopaque Cerebral (methylglucamine salt of metrizoic acid with the addition of small amounts of  $\text{Ca}^{++}$ ).

*Leakage of protein bound dye* The Evan's blue started to diffuse into the tissue within 10 to 20 minutes of its intravenous injection. The leakage started in the periphery of the deposit area where the microcirculation was first restored, continuing centripetally and resulting in homogeneous blue staining of the deposit area when the microcirculation had recovered in the whole area.

The disturbances in permeability in the deposit areas of the hamster cheek pouch caused by different contrast media examined are illustrated in Fig 5. Table 3 and Fig 6 depict the intensity of staining of the various deposit areas expressed in  $\mu\text{A}$  and measured after the colour intensity had become homogeneous in the whole deposit area. High values indicate a high degree of light absorption, i.e. a relatively large amount of dye had leaked through the microvessels into the perivascular tissues where it was retained. In all experiments larger concentrations of contrast medium gave rise to a greater concentration of dye. A definite difference in colour intensity caused by the three commercially used preparations, Isopaque 260, Isopaque Cerebral, and Urografin 60% with an iodine content of 260 mg/ml, 280 mg/ml, and 291 mg/ml, respectively, could not be demonstrated. The lowest concentration of Urografin able to

permeability. The last film in the single experiments was obtained at least half an hour after full restitution of microvascular flow velocity to avoid the error inherent in possible absence of staining in the deposit area caused by insufficient microvascular flow.

The lowest concentration of the different contrast media capable of producing an increased permeability recognizable by this photometric method was titrated out by dilution of the commercial preparations of Urografin, Isopaque 260 and Isopaque Cerebral. By the same method the lowest concentration of the three preparations just able to cause momentary circulatory standstill in a small venule was identified.

### Results

The disturbances in the microcirculation caused by the various contrast media as assessed by vital microscopy appeared to be in accordance with earlier reports by BRÄNEMARK *et coll.* Striking differences were recorded when the toxic effects of a contrast medium were compared with the equimolar sodium chloride solution. Sodium chloride solutions higher than 4.5 % caused immediate precipitation of the tissue proteins, and the tissue in the deposit area became structureless and shrunken, only the circulation in the larger arterioles and venules passing through the deposit area being preserved. After the application of salt solutions lower than 4.5 % more detailed analysis of the microvascular events could be performed. The blood immediately became coarse and granular in appearance, the blood cells being dark, crenated and deformed. The content of the vessels never appeared brilliantly red, structureless or homogeneous as after the administration of contrast media, the red cell boundaries could be identified. Increased transparency in the deposit area — as after the administration of contrast media — was never observed.

After the injection of the sodium chloride solutions, the rate of flow immediately decreased with subsequent circulatory standstill, first in the small venules then in the capillaries and the large venules and finally in the arterioles. The time required for restitution of flow to the original circulatory values varied with the concentration of the salt solution (Fig. 3). In a comparison of the damaging effect of contrast medium and equimolar salt solution — as manifested by the time elapsing from administration of the medium to restitution of flow to the original circulatory values — the salt solutions always produced less injury than the contrast medium (Figs 3 and 4). After recovery of the circulation the vessels presented signs of toxic reaction *viz.* an increasing number of granulocytes sticking to and sliding along the vessel wall. Single thrombi adhering to the vessel wall were never observed.

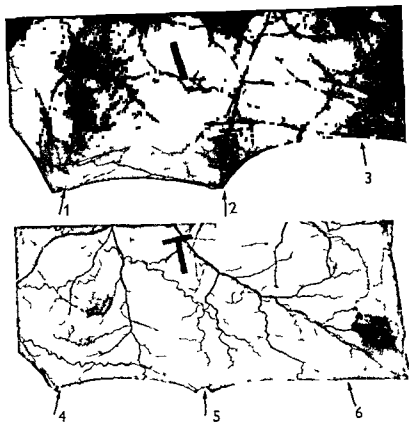


Fig 5 Increased capillary permeability in the cheek pouch of the hamster as indicated by escape of protein bound Evans blue into the tissue. The contrast media administered in the various deposit areas were: Perjodal U (1) Urografin 45 % (2) Isopaque 260 (3) Isopaque 350 (4) Urografin 30 % (5) and Perjodal H (6)



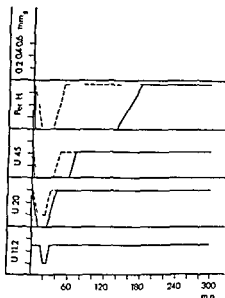


Fig 4 Diagrammatic representation of changes in microvascular flow velocities after administration of Urografin 11.2%, Urografin 20%, Urografin 45% and Peridol H. Unbroken line represents the contrast medium as compared with the equimolar sodium chloride solution (dotted line).

produce an increase in vascular transfer as demonstrable by this method was, in a series of experiments, about 20%, corresponding to an iodine content of 97 mg/ml. The same values were recorded for Isopaque 260 and Isopaque Cerebral. Sodium chloride solutions in any concentration between those of Tyrode's solution and a 4.5% solution produced no increased blue staining in the deposit area. Increased transparency as observed after deposition of contrast media was not observed.

### Discussion

The first contrast media introduced were inorganic compounds of high systemic and local toxicity. Later media of the type two molecular organic compounds were found to be better tolerated although a high degree of toxicity and frequent untoward reactions continued to be encountered. With the introduction of the three iodinated organic water soluble contrast media of the type diatrizoate, metrizoate and iothalamate, the frequency of side reactions was further reduced. Nonetheless toxic reactions of varying intensity are still reported and the ideal contrast medium has as yet not been synthesized.

Various techniques have been employed to test the toxicity of contrast media towards different organs and tissues. These test methods include registration of changes in circulatory dynamics in man as well as in experimental animals after intravascular administration of the different media as reflected by alterations in blood pressure, heart rate, ECG, and peripheral blood flow (PATTINSON 1962,

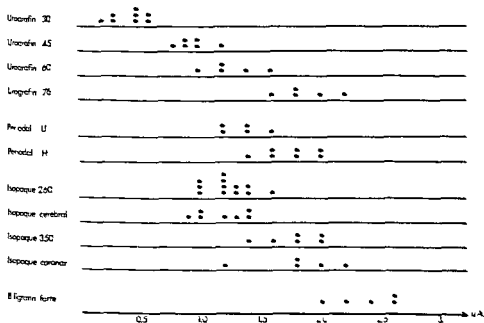


Fig 6 Diagrammatic representation of increase in capillary permeability as shown in Table 3. The abscissa represents difference in light intensity between the surrounding region and deposit area measured on colour photographs of the cheek pouch of the hamster with a microammeter.

Table 3

*Difference in light transmission measured with a microammeter and expressed in  $\mu A$  — Each figure represents the arithmetic mean value for 10 measurements between the deposit area and adjacent tissue regions*

| Contrast medium   | Mean deposit |     |     |     |     |     |     |     |  |
|-------------------|--------------|-----|-----|-----|-----|-----|-----|-----|--|
| Urografin 30 %    | 0.5          | 0.6 | 0.3 | 0.6 | 0.5 | 0.3 | 0.5 | 0.2 |  |
| Urografin 45 %    | 1.0          | 1.2 | 1.0 | 0.9 | 0.9 | 0.8 |     |     |  |
| Urografin 60 %    | 1.2          | 1.6 | 1.4 | 1.0 | 1.2 |     |     |     |  |
| Urografin 76 %    | 2.0          | 1.6 | 2.2 | 1.8 | 1.8 |     |     |     |  |
| Periodal H        | 1.6          | 1.8 | 1.8 | 2.0 | 2.0 | 1.6 | 1.4 |     |  |
| Periodal U        | 1.4          | 1.6 | 1.4 | 1.2 | 1.2 |     |     |     |  |
| Isopaque 260*     | 1.0          | 1.2 | 1.3 | 1.2 | 1.2 | 1.4 | 1.0 | 1.6 |  |
| Isopaque Cerebral | 1.4          | 1.4 | 1.0 | 1.3 | 1.0 | 0.9 | 1.2 |     |  |
| Isopaque 350      | 1.8          | 2.0 | 1.4 | 2.0 | 1.8 | 1.6 |     |     |  |
| Isopaque Coronar  | 1.2          | 2.0 | 1.8 | 2.2 | 1.8 |     |     |     |  |
| Isopaque 260**    | 1.3          | 1.2 | 1.4 | 1.0 |     |     |     |     |  |
| Biligradin forte  | 2.0          | 2.4 | 2.2 | 2.6 | 2.6 |     |     |     |  |

\* Balanced sodium metrizoate (commercial preparation)

\*\* Pure sodium metrizoate



leaking dye at the site of injury seems to be a reliable method of comparing the permeability changes caused by the different contrast media and salt solutions (WILHELM & MASON 1960)

Fig 5 and Table 3 indicate that the contrast media were more toxic the higher their concentration. No significant difference in toxicity between the different solutions of metrizoate and diatrizoate with the same iodine concentration could be demonstrated with the test model used in the present investigation. This comparison was done by titrating out the lowest concentration of the different contrast media just able to cause demonstrable local leakage of dye. The iodine concentrations of the three solutions examined (Urografin, Isopaque Na/Ca/Mg and Isopaque Cerebral) were found to be in the range 97 mg/ml to 102 mg/ml.

Even for contrast media with slightly different iodine concentration, Urografin 60 %, Isopaque 260 Na/Ca/Mg and Isopaque Cerebral, with an iodine content of 291 mg/ml, 260 mg/ml and 280 mg/ml, respectively, no difference in toxicity could be demonstrated with certainty. It should be mentioned in this context that SALVESEN *et coll* were able to demonstrate by means of the blood brain barrier test even very small differences in composition between various contrast media.

The sodium and N methyl glucamine salts of the various contrast media have demonstrated a better tolerability of the N methyl glucamine salts than the sodium salts in investigations of the pharmacologic action of different cations, this is specially true as regards the toxicity to the myocardium (FISCHER & ECKSTEIN 1961, FISCHER *et coll*, GENSI & DIGIORGI, HILAL, BROWN *et coll*, PAULIN). No such difference could be demonstrated with this test model. This is in agreement with the investigations of LINDGREN *et coll* (1967) who in registering the blood flow in the femoral artery of the cat, were unable to demonstrate any significant difference as regards the vascular activity between solutions of Urografin, metrizoate Na, and metrizoate Na with the addition of small amounts of Ca and Mg, provided the solutions were adjusted so that they contained the same amount of iodine/ml.

The hypertonicity of contrast media is an important factor to be considered in any investigation of systemic and local toxicities. The injection of hypertonic solutions is known to provoke marked circulatory changes in mammals (WALCOTT & DEYRUP 1948, READ *et coll* 1960, BUSFIELD *et coll* 1962, GIAMMONA *et coll* 1963, HILAL, LINDGREN *et coll*). The observations reported in the present paper give only partial support to the hypothesis that the hypertonicity will explain most of the pharmacodynamic effects of contrast media. The medium is a sodium chloride solution as measured by osmometry (Figs 3 and 4). This is not in agreement with the results of ALMEN & WIEDEMAN (1968) who investigated the effect of contrast media on the microcirculation in the wing of the bat.

GENSINI & DIGIORGI 1964, FODA et coll 1965, TINDALL et coll 1965, ISERI et coll 1965, BROWN et coll 1965, HILAL 1966, JACOBSSON & PAULIN 1967, BROWN et coll 1967, LINDGREN et coll 1968)

The kidneys and the spinal cord may be used as test organs with high doses of contrast medium and repeat injections (KILLEN & LANCE 1960, BERNSTEIN et coll 1962, RHEA et coll 1964, 1965, MARGOLIS & YERASIMIDES 1966)

The registration of bradycardia during carotid angiography has been demonstrated to be a simple but highly sensitive method of comparing the toxicity of different contrast media (GREITZ 1956, FISCHER et coll 1962, GREITZ & TORNFELL 1967). The toxicity of the various contrast media has also been examined by observing the changes they cause in the microcirculation of different animals after intravascular injection (JOHNSON & KNISELY 1962, WIEDEMAN 1963, BRÄNFMARK et coll ), and by noting the effect on the endothelium (ZINNER & GOTTLOB 1959, MERSEREAU & ROBERTSON 1961, MCCONELL & MERSEREAU 1964, AUSMAN et coll 1964). Several observers have demonstrated increased permeability of a vascular bed supplied by an artery into which contrast medium had been injected (BROMAN & OLSSON 1948, STEINWALL 1958, HARRINGTON & WIEDEMAN 1965, SALVESBY et coll 1967).

It thus appears that extensive investigations have been performed to evaluate the toxicity of contrast media towards organs and tissues. In evaluating the causes of these side effects interest is directed to the significance of the cation, the anion and the hypertonicity of the solution. It seems reasonable to suppose that different organs and tissues are sensible to the components of the contrast media to a varying degree. This suggests the investigation of new test models and methods and the definition of more parameters to indicate the toxicity of contrast media.

The present investigation of the local toxic effect of contrast media in concentrations supplied by the manufacturer and used in clinical routine work indicates that all cause local injury to the endothelial barrier as manifested by increased permeability. The hamster cheek pouch appears to be well suited and of adequate sensitivity for the purpose. The estimation of the effect of substances on the capillary permeability by determining protein bound dye leakage into the tissues in the deposit area was a method originally described by RAMSDALL (1928). The technique is most widely used in investigating disturbances in capillary permeability (SPECTOR 1958). The test has been used in rabbits, mice, guinea pigs, rats and even man (MENKIN 1936, MILES & MILES 1952, SPECTOR & WILLOUGHBY 1957, SPARROW & WILHELM 1957, STEWART & BLISS 1957, JUDAH & WILLOUGHBY 1962, WILHELM 1962). Since in this investigation the injury in the microvascular area is induced by a standard amount of test substance (0.05 ml) and since the test region is uniform as regards microvascular anatomy and physiology, the estimation of differences in colour intensity of

leaking dye at the site of injury seems to be a reliable method of comparing the permeability changes caused by the different contrast media and salt solutions (WILHELM & MASON 1960)

Fig 5 and Table 3 indicate that the contrast media were more toxic the higher their concentration. No significant difference in toxicity between the different solutions of metrizoate and diatrizoate with the same iodine concentration could be demonstrated with the test model used in the present investigation. This comparison was done by titrating out the lowest concentration of the different contrast media just able to cause demonstrable local leakage of dye. The iodine concentrations of the three solutions examined (Urografin, Isopaque Na/Ca/Mg and Isopaque Cerebral) were found to be in the range 97 mg/ml to 102 mg/ml.

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It might be suggested that the disturbances in the microcirculation caused by the hypertonic solutions in the deposit areas alone could account for the increased permeability of the microvessels. Thus, HARRINGTON et coll (1966) produced damage to the blood brain barrier by injecting hypertonic saline in the carotid artery of the dog. It appears, however, from Fig 3 that sodium chloride solutions in a concentration higher than 3.85 % cause more marked microcirculatory disturbances, as manifested by the time of microcirculatory standstill, than Urografin 30 %. In spite of this fact a measurable disturbance in permeability could not be demonstrated after the administration of hypertonic sodium chloride solutions up to a concentration of 4.5 %. This further supports the conclusion that the osmolarity is at least not solely responsible for the tissue injury caused by contrast media.

### Conclusion

The toxicity of contrast media has been investigated by their administration to the hamster cheek pouch. A comparison of toxicity between contrast medium and the equimolar sodium chloride solution was performed. The investigation was based on the analysis of microvascular structure and function because tissue injury is caused by and manifests itself in disturbances in the microcirculation. The hamster cheek pouch proved to be well suited for investigations of contrast media toxicity, simple and easy to handle and provided with an adequate sensitivity level. The present report is part of a series of investigations on contrast media and tissue injury. It is apparent that all media in the concentrations supplied by the manufacturer and employed in clinical work are injurious to the tissues. The test methods employed to evaluate toxicity with application of the media directly in the tissue are admittedly not directly comparable to the clinical use of radiopaque media. The aim of this investigation, however, has been to elucidate and evaluate the possible untoward effects of the various media commonly in use today. It is believed that the primary value of the experiments lies in their use as a test method.

In the part of the present investigation concerning analysis of disturbances in permeability caused by the different contrast media, it has been possible to use a standard dose of contrast medium, a standard photographic technique and a standard technique for evaluation of tissue staining. It has thus been possible to develop a semiquantitative method for comparison of the toxicity attached to different contrast media.

Vital microscopy as reported in this investigation and earlier by BRÅNEMARK et coll was found to be a more sensitive method than analysis of disturbances in

permeability in recognizing and evaluating the degree of tissue injury caused by radiopaque media. The hypertonicity of the contrast media could not be held responsible for all the toxic effects demonstrated by this test model.

### Acknowledgements

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### SUMMARY

The toxicity of contrast media and hypertonic sodium chloride solutions were investigated in the tissue of the cheek pouch of the hamster as reflected by disturbances in the microcirculation and changes in the microvascular permeability. It appeared that the hypertonicity of the contrast media was responsible for some of the microvascular disturbances but did not induce a recognizable increase in capillary permeability.

### ZUSAMMENFASSUNG

An den Backentaschen von Hamstern wurde die Toxizität von Kontrastmitteln und von hypertonschen Kochsalzlosungen hinsichtlich einer gestörten Mikrozirkulation und einer Veränderung der Permeabilität der Kleingefässe studiert. Es zeigte sich, dass die Hypertonizität der Kontrastmittel die Störungen der Mikrozirkulation veranlasste, aber nicht zu einer erhöhten Permeabilität der Kapillaren führte.

### RÉSUMÉ

La toxicité des moyens de contraste et des solutions hypertoniques de chlorure de sodium a été étudiée dans le tissu de la poche de joues du hamster en observant les perturbations de la microcirculation et les modifications de la perméabilité microvasculaire. Il est apparu que l'hypertonie des milieux de contraste était responsable de certaines perturbations microvasculaires mais ne donnait pas lieu à une augmentation appréciable de la perméabilité capillaire.

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## SPONTANEOUS CLOSURE OF ARTERIOVENOUS FISTULAE FOLLOWING PERCUTANEOUS RENAL BIOPSY

An experimental investigation in the rabbit

by

LEIF EKEUND

Only a few cases of spontaneous closure of renal arteriovenous fistulae secondary to renal biopsy have been reported (BENNETT & WIENER 1965, NILSSON & ROSS 1967, EKEUND & LINDHOLM 1971). EKEUND (1970) demonstrated closure of such fistulae in two experimental cases. Five cases of spontaneous closure of fistulae caused by trauma other than biopsy (gunshot wounds, blunt trauma) have recently been published (HALPERN 1969). This tendency to spontaneous closure must be an important factor when deciding the treatment of postbiopsial arteriovenous fistulae (which are more common than formerly believed (EKEUND 1970)). An attempt to evaluate its frequency therefore appeared reasonable and prompted the present investigation.

*Material and Methods* Forty-one rabbits, weighing 2.0 to 3.0 kg, were used. One kidney was punctured twice and selective nephroangiography performed a week later. The technical details of kidney puncture and angiography were

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Fig 1 a) Right selective nephroangiography one week after kidney puncture. Arteriovenous fistula in middle part of kidney with good contrast filling of renal vein as well as of inferior vena cava b) Two months after renal puncture. Closure of fistula

presented in a previous paper (EKEFLUND 1970). Renal tissue in the present investigation was also sometimes aspirated in connection with the punctures. The needle used for the kidney puncture in the present series was somewhat larger (diameter 0.6 mm) than the one previously used (0.4 mm) in order to produce as many arteriovenous fistulae as possible.

Arteriovenous fistulae were present at angiography one week after puncture in 20 rabbits. A second selective nephroangiography was performed two months after puncture with catheterization from the opposite femoral artery in these animals.

## Results

Closure of the fistulae could be demonstrated in 14 of the 20 cases (70%) at repeat angiography two months after puncture (Fig 1, a and b). The fistulae had diminished considerably in size in 3 cases and were roughly the same size as one week after puncture in the last 3 cases (Figs 2, a and b and 3).



Fig 2 a) Arteriovenous fistula between artery and vein  
b) Two months later contrast filling



Fig 3 Left selective nephroangiography two months after renal puncture. Persistent arteriovenous fistula in lower pole of kidney. Infarctions laterally and cranially.

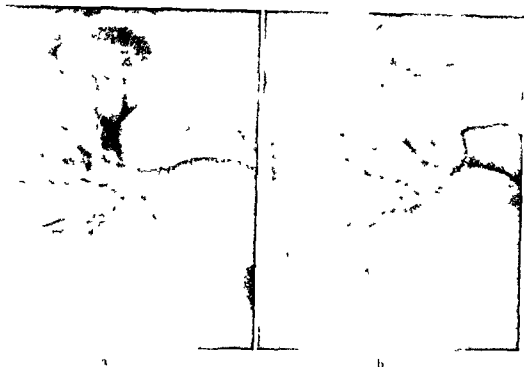


Fig 4 a) Right selective nephroangiography one week after renal puncture. Arteriovenous fistula in cranial pole of kidney with contrast filling of renal vein and inferior vena cava. b) Two months after puncture. Closure of fistula. Small scars cranially and laterally.

There seemed to be no correlation between the size of the fistulae and the tendency to spontaneous closure — even large fistulae closed. No renal infarcts were evident at the first angiography one week after puncture. Infarcts appeared in three kidneys with closed fistulae at the second angiography (Fig 4, a and b) and in one case in which the fistula was persistent. Small irregularities of the arteries were sometimes present at the site of the closed fistula, but arterial occlusions were never apparent.

All animals were in good condition during the experiment, except for moderate paresis of the hindleg on the side of the first catheterization in a few rabbits.

### Discussion

The results of this experimental investigation point to the fact that spontaneous closure of renal arteriovenous fistulae secondary to renal biopsy is common, though it must be stated that the coagulation ability in the rabbit is somewhat higher than in man. Closure of similar fistulae has also been reported in clinical materials. BENNETT & WIENER (1965) reported disappearance of

fistulae in 3 out of 7 cases at repeat angiography NILSSON & ROSS (1967) described closure of bilateral fistulae EKELOUND & LINDHOLM (1971) presented 5 cases of spontaneous closure out of 7 patients with renal arteriovenous fistulae following renal biopsy No infarction occurred in any of these 5 cases Disappearance of renal arteriovenous fistulae produced by trauma other than biopsy (gunshot wounds, blunt trauma) was described in 5 cases by HALPERN (1969), who also claimed that thrombosis must be the mechanism of cure

The treatment of traumatic renal arteriovenous fistulae is usually considered to be surgical (KAUFMAN et coll 1965, GOMES & BERNATZ 1970) The facts mentioned however suggest that more conservative treatment might be wiser and control angiography performed after one or two months If at that time the fistula should still persist or be larger or symptoms and signs of cardiac incompenstation or hypertension appear, surgical intervention may be necessary These considerations should at least be relevant with renal arteriovenous fistulae secondary to renal biopsy, which are usually symptomless (MALDONADO & SHEPS 1966)

## SUMMARY

An experimental investigation in the rabbit of the tendency to spontaneous closure of renal arteriovenous fistulae following renal biopsy is presented Repeat nephroangiography two months after kidney puncture in 20 rabbits with proved fistulae revealed closure in 14 (70 per cent) The results indicate that treatment of such fistulae should primarily be conservative and properly controlled by nephroangiography

## ZUSAMMENFASSUNG

Es wurden Versuche am Kaninchen . . . . .

Vierzehn Kaninchen  
konservativ behandeln soll und lediglich weiter mit Nephroangiographie kontrolliert

## RÉSUMÉ

L'auteur présente une recherche expérimentale sur le lapin concernant la tendance à la fermeture spontanée des fistules artério-veineuses rénales après biopsie rénale Une néphroangiographie faite deux mois après ponction rénale chez 20 lapins présentant des fistules prouvées a montré la fermeture des fistules chez 14 lapins (70 pour cent) Ces résultats montrent que le traitement de ces fistules devrait initialement être conservateur et contrôlé convenablement par néphroangiographie



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## HEMODYNAMIC EFFECT OF CONTRAST MEDIUM IN ARTERIOGRAPHY OF LEGS

by

ERIK BOIJSEN, INGE DAHN and TORGIL HALLBOOK

The hemodynamic effect of intraarterial injection of contrast medium into various organs has been investigated both experimentally and clinically. The angiographic technique, in particular the volume and the rate of injection of the contrast medium, must be varied according to the hemodynamic characteristics of the organ to be examined. The vascular beds differ, for example, with respect to peripheral resistance and arteriovenous anastomoses so that the hemodynamic effect of an injected contrast medium can be expected to vary from one organ to another. It is therefore difficult to draw generally valid conclusions from the findings in a given organ. This may perhaps explain certain differences of opinion on the effect of contrast medium on peripheral

hemodynamics. The characteristic reaction is a reduction of the blood pressure and an increase in the cardiac rate and output (AMUNDSEN et coll 1956, BROWN et coll 1965, FRIESINGER et coll 1965,

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Injection of a water-soluble contrast medium into the heart, aorta or peripheral arteries immediately produces hemodynamic changes. The characteristic reaction is a reduction of the blood pressure and an increase in the cardiac rate and output (AMUNDSEN et coll 1956, BROWN et coll 1965, FRIESINGER et coll 1965,

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Table 1

*Twelve plethysmographic blood flow measurements in six normal legs performed during angiography at rest. The columns denoted with 'difference' give the differences between the original flow and respectively the lowest and highest flow values obtained after the injection of contrast medium*

| Original flow before injection of the contrast medium | Flow values (in ml/min x 100 ml) and time of appearance (in seconds) of lowest and highest flow after injection of the contrast medium, with differences in relation to the original flow |            |                    |                    |            |                    |
|---|---|------------|--------------------|--------------------|------------|--------------------|
|   | Lowest flow value   | Difference | Time of appearance | Highest flow value | Difference | Time of appearance |
| 3.3   | 2.9   | 0.4        | 6                  | 8.7                | 5.4        | 42                 |
| 2.9   | 2.7   | 0.2        | 6                  | 15                 | 12.1       | 42                 |
| 6.2   | 4.4   | 1.8        | 12                 | 15                 | 8.8        | 35                 |
| 6.2   | 5.1   | 1.1        | 4                  | 17                 | 10.8       | 30                 |
| 3.8   | 2.0   | 1.8        | 7                  | 18                 | 14.2       | 30                 |
| 2.7   | 1.8   | 0.9        | 14                 | 8.8                | 6.1        | 42                 |
| 3.1   | 2.6   | 0.5        | 8                  | 10.2               | 7.1        | 38                 |
| 1.9   | 1.6   | 0.3        | 14                 | 17                 | 15.1       | 36                 |
| 3.0   | 2.3   | 0.7        | 14                 | 18                 | 15.0       | 48                 |
| 2.6   | 2.0   | 0.6        | 10                 | 16                 | 13.4       | 42                 |
| 4.0   | 1.0   | 3.0        | 15                 | 13                 | 9.0        | 35                 |
| 4.3   | 2.9   | 1.4        | 7                  | 19                 | 14.7       | 35                 |
| $\bar{x}$ 3.6   |   | 1.0        | 9.7                |                    | 10.9       | 40                 |
| SD 1.46   |   | 0.86       | 3.88               |                    | 3.56       | 1.8                |

KLOSTER et coll 1966, ZSEBOK & SZLAVY 1966) These reactions can be explained by the hypertonicity of the contrast medium with consequent peripheral vasodilatation and uptake of fluid from the extracellular space with consequent hypervolemia (KLOSTER et coll 1966, BRISTOW et coll 1967) Experimental investigations have shown that the contrast medium produces an immediate reduction in the volume of the red blood cells (McINTOSH et coll 1967)

Experimental investigations in animals have shown that an intraarterial injection of a contrast medium always produces vasodilatation, and thereby an increase in blood flow in the area in question (LINDGREN & TORNELL 1958, READ et coll 1960, HILAL 1966) Some authors claim that injection of a contrast medium produces only vasodilatation (LINDGREN & TORNELL 1958, LINDGREN et coll 1968, HILAL 1966)

The earlier belief that contrast media cause arterial spasm (FOLTZ et coll 1952, JEPSON & SIMEONE 1953, SHAW 1956) has not been verified with modern contrast media This spasm, which occurred following the use of more toxic contrast agents

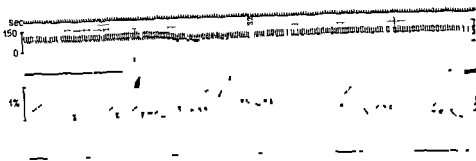


Fig 1 Recording of blood pressure (in mm Hg) and plethysmographic recording of blood flow during angiography. Consecutive flow values in  $\text{ml/min} \times 100 \text{ ml}$  for each period of venous

of the arterial branches at the level of the strain gauge

was probably not functional, however, but due to local vascular injury (WIEDEMAN 1963, MCCONELL & MERSEREAU 1964, BROMAN & OLSSON 1956, GREYSON et coll 1961, FUJII et coll 1963). Though the occurrence of arterial spasm is doubted by most authors, WIEDEMAN (1963) demonstrated brief, rapid contractions in the wing of the bat following intraarterial injection of contrast medium. LINDGREN & TORNELL (1958) claimed that the initially observed red

reduction in flow, which was followed by a more prolonged increase in flow and fall in blood pressure. Other authors, who also observed such a reduction in flow, claim like MARSHALL & SIEPHERD that it must be due to an agglutination of the red blood cells (READ et coll 1959, 1960, WIEDEMAN 1963, MCINTOSH et coll 1967). SAKO (1963) suggested that the reduction of the flow could be due to

First, when physiologic saline was injected, the rise lasted only during the actual injection but when contrast medium was injected it persisted a few seconds longer. They ascribed the rise in pressure to a brief increase in the peripheral resistance, which they, like SAKO (1963), thought might be due to the increased viscosity.

The purpose of the present investigation was to find out, by simultaneous measurements of blood pressure and blood flow during clinical angiography, how



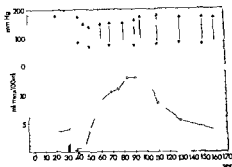


Fig 3 Blood pressure and blood flow in a normal leg at angiography during rest  
 ▲ denotes the time and duration of the contrast medium injection  
 ▭ and ▮ indicate the time when the contrast medium reached respectively the main artery and the arterial branches at the level of the strain gauge

4 cases made via a catheter placed percutaneously in the brachial artery, with the tip in the axillary artery. In one case, the central blood pressure was recorded via a catheter placed in the brachial artery with the tip in the axillary artery and the peripheral blood pressure in the leg with a catheter in the superficial femoral artery with the tip about 20 cm below the inguinal ligament. The contrast medium was in this case injected via a catheter passed through the contralateral femoral artery.

*Measurement of blood flow* The blood flow was measured by venous occlusion plethysmography with a strain gauge plethysmograph (HALLBOOK et coll 1970, DAHN & HALLBOOK 1970). The patient lay supine on the examination table with the calves just below the level of the heart. The strain gauge was placed around the largest part of the calf about 15 cm below the knee, with the occlusive cuff immediately above the knee. The blood flow was measured continuously before, during and after the injection of contrast medium during 5- to 7 second periods of venous occlusion at intervals of 3 to 4 seconds.

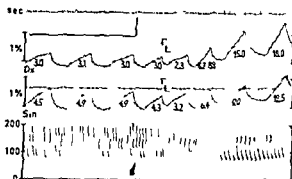
The blood flow curves were recorded on the Mingograf simultaneously with the other variables mentioned. Since the times of exposures and injections were recorded, it was possible to determine the exact point in time when the contrast medium reached respectively the main arteries and the peripheral branches in those segments where the flow was measured. It was therefore possible to study the changes in flow and pressure, on one hand, and the flow of the contrast medium, on the other hand, thus enabling a correlation and a study of the effect of the injection on the vascular bed in the area examined.

In the course of angiography, the blood flow was measured during rest and during reactive hyperemia. The reactive hyperemia was produced by arterial occlusion and exercise during ischemia. The contrast medium was injected 10 to 15 seconds after the end of arterial occlusion, i.e. as closely as possible to the maxi-



Fig 2 Recording of blood pressure and plethysmographic recording of blood flow during simultaneous angiography of both legs. Increase in blood pressure on injection of contrast medium and decrease when the flow values increase. Arterial obliteration in the left leg and arterial stenosis of the right.

Flow values, calibration and symbols as in fig 1



an intraarterial injection of contrast medium affects the vascular bed of the legs in patients with normal vessels as well as patients with occlusive disease

**Material** This consisted of patients investigated with arteriography of the lower limbs because of arterial disease, 25 limbs of 15 patients being examined. The circulation was normal in six limbs and two limbs had had surgery with vascular reconstruction and had patent shunts in the thigh, the remainder of seventeen limbs displayed atheromatous changes of varying severity and varying degrees of impairment of the arterial circulation.

### Methods of investigation

**Angiography** The catheter, which had a tapered end and side holes, was introduced percutaneously into the femoral artery and placed with its tip just above the aortic bifurcation, 25 to 35 ml Isopaque Cerebral were injected with a pressure injector at a rate of 15 to 20 ml/second. The time of injection of contrast medium and the exposures were recorded on a Mingograf. Repeat injections of the same amount of contrast medium at the same rate were made in order to demonstrate the entire arterial system from the distal part of the lumbar aorta to the arteries of the foot. This required at least four injections. The interval between consecutive injections was at least 10 minutes.

**Measurement of blood pressure** A catheter placed in an artery was connected with an Elema pressure transducer, and the blood pressure together with other variables were recorded on a Mingograf. The pressure catheter was introduced into the same femoral artery, distal to the catheter for the injection of contrast medium (one case), or in the contralateral femoral artery (3 cases). The tip of the pressure catheter was placed a few centimeters distally to the tip of the catheter used for the contrast medium. Measurements of blood pressure were in

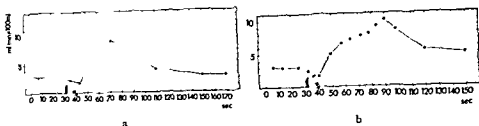


Fig 5 a) Blood flow at angiography of a normal leg b) Blood flow at angiography of a leg with arterial obliteration The appearance of the flow maximum is delayed  
Symbols as in fig 3

then 30 to 40 mm Hg systolic and 20 to 30 mm Hg diastolic below the original values (Fig 2). The pressure then gradually rose, to return to its original level 70 to 80 seconds after the start of injection of contrast medium (Figs 1 and 3). The flow in the calf always reached a minimum 5 to 10 seconds before the central pressure while the blood pressure was still falling or before it had begun to fall. By the time the blood pressure had reached a minimum, the blood flow had always increased and the flow values were generally four fold. The maximal flow in the legs with normal arteries always occurred before the blood pressure returned to its original level. The flow and the pressure returned to these levels at roughly the same time after injection of the contrast medium.

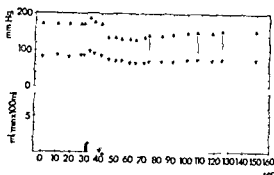
*Simultaneous measurements of flow in arms and legs* Measurements of the flow in one arm and one leg were made during angiography of the limb in order to study the effect of the central pressure on flow (Fig 4).

The blood flow in the arm, in 50 % of the examinations, increased slightly about 10 seconds after the injection of contrast medium into the aorta. This occurred during the decreased flow in the leg. Afterwards, the flow in the arm decreased at the same time as it increased in the leg. The flow in the arm became normal 50 to 60 seconds after the injection and varied synchronously with changes in the central blood pressure. In the arm, the increase in flow was never of the same magnitude as that observed in the leg after injection of contrast medium.

*Flow in legs with obliterated arteries* In legs with obliterated main arteries the reduction of the flow was recorded in legs with normal arteries reduced to about 55 % of the original value. The average reduction in 24 examinations of nine legs was 1.5 ml/minute  $\times$  100 ml (range 0.2 ml and 2.7 ml) (Table 2). The flow was minimal 15 seconds after the start of injection, the increase in flow occurred gradually and was less marked than in normal legs. The

Fig 4 Blood flow in the arm (\*) and in the leg (O) at angiography of the leg. The blood pressure was measured in the axillary artery

Symbols as in fig 3



imum of flow during the reactive hyperemia. When the flow in one leg differed from that in the other leg of a given patient, it was usually the maximal flow in the leg with the lower flow rate that was used. Instead of the contrast medium, and using the same technique, a corresponding amount of normal saline was injected in five patients and 5 % saline in one patient.

In order to study the general and local reactions to the injected contrast medium, the flow in one arm and in the leg were measured simultaneously in two patients, while the central blood pressure was recorded via a catheter in the other arm. When measuring the flow through the arm, the strain gauge was placed round the lower arm, 10 cm below the olecranon, and the cuff was placed round the upper arm.

## Results

### *Effect of the contrast medium during rest*

*Flow through normal arteries.* Within 5 to 10 seconds of the injection of contrast medium into the aorta, the blood flow in the calf at rest fell to about 70 % of its original level. In 12 examinations of six legs, the average decrease in flow was 1.0 ml/minute  $\times$  100 ml (Table 1). The flow rate was lowest about 10 seconds (range 4 to 14 seconds) after the beginning of injection.

The flow rapidly rose, after the initial reduction, which was reflected by an abrupt rise in the plethysmographic recording. The time of increase in flow was 10 to 20 seconds from the beginning of injection of the contrast medium, and maximal flow occurred 40 to 50 seconds after the injection (Fig 1).

The contrast medium regularly reached the main artery and branches about 3 to 4 seconds before the flow was at its minimum. No contrast medium was demonstrable in the arteries at maximal flow.

The injection of contrast medium was usually followed by a 10 to 20 mm Hg rise in pressure within a few seconds. After a further 4 to 5 seconds, the blood pressure fell to its minimal level, 20 to 30 seconds after the injection, which was

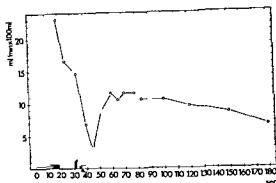


Fig 6 Blood flow at angiography during reactive hyperemia of a normal leg

— denotes end of 3 minutes ischemia

▲ denotes time and duration of contrast medium injection

┌ and └ indicate the time when the contrast medium reached respectively the main artery and the arterial branches at the level of the strain gauge

leg, a finding which is in agreement with the angiographic observation that the contrast medium passed more rapidly on the healthy side

The increase in flow after injection of contrast medium was smaller in legs with arterial obliteration and reached a maximum 15 to 20 seconds later. In a few patients with marked atherosclerotic disease, the increase in flow did not reach a maximum until 90 to 110 seconds after the injection and it persisted longer (Table 2, Fig 5b)

#### *Effect of injection of contrast medium during reactive hyperemia*

In order to find out whether the decrease in flow following the injection of contrast medium occurred also in an area where the vessels were dilated, we studied the changes in flow at angiography during reactive hyperemia after exercise during ischemia

*Flow through normal arteries* In the examination of legs with normal arteries, the contrast medium was injected during maximal flow, i.e. 10 to 15 seconds after the end of ischemia. The flow diminished 3 to 5 seconds from the beginning of the injection of contrast medium and some seconds after the contrast medium had reached the level of the strain gauge, in some instances down to 20 to 25 % of the preceding value (Fig 6). The flow reached a minimum about 10 seconds after the injection. The decrease in flow was brief and soon returned to normal during reactive hyperemia, and immediately afterwards increased as a consequence of hyperemia due to the contrast medium

Changes in blood flow in relation to the changes in blood pressure on injection of contrast medium are given in Fig 7. As during rest, the decrease during reactive hyperemia occurred before the fall in pressure and immediately after the injection

Table 2

*Twenty four plethysmographic measurements of blood flow in nine legs with arterial obliteration performed during angiography at rest. The columns denoted with 'difference' give the differences between the original flow and respectively the lowest and highest flow values obtained after the injection of contrast medium*

| Original flow before injection of the contrast medium | Flow values (in ml/min $\times$ 100 ml) and time of appearance (in seconds) of lowest and highest flow after injection of the contrast medium, with differences in relation to the original flow |            |                    |                    |            |                    |
|---|--|------------|--------------------|--------------------|------------|--------------------|
|   | Lowest flow value  | Difference | Time of appearance | Highest flow value | Difference | Time of appearance |
| 44  | 18   | 26         | 10                 | 46                 | 02         | 70                 |
| 55  | 23   | 32         | 10                 | 65                 | 10         | 60                 |
| 14  | 29   | 15         | 15                 | 115                | 71         | 55                 |
| 48  | 32   | 16         | 14                 | 125                | 77         | 40                 |
| 45  | 43   | 02         | 12                 | 11                 | 65         | 50                 |
| 30  | 16   | 14         | 6                  | 10                 | 70         | 60                 |
| 26  | 18   | 08         | 10                 | 70                 | 44         | 50                 |
| 29  | 19   | 10         | 15                 | 75                 | 46         | 50                 |
| 23  | 10   | 13         | 18                 | 10                 | 77         | 60                 |
| 39  | 33   | 06         | 20                 | 18                 | 141        | 50                 |
| 39  | 26   | 13         | 12                 | 13                 | 91         | 55                 |
| 23  | 17   | 06         | 8                  | 65                 | 42         | 55                 |
| 30  | 12   | 18         | 22                 | 75                 | 45         | 110                |
| 35  | 10   | 25         | 30                 | 87                 | 52         | 95                 |
| 37  | 10   | 27         | 25                 | 75                 | 38         | 90                 |
| 29  | 08   | 21         | 25                 | 77                 | 48         | 65                 |
| 29  | 10   | 19         | 15                 | 77                 | 48         | 60                 |
| 30  | 12   | 18         | 15                 | 75                 | 45         | 90                 |
| 46  | 37   | 09         | 6                  | 10                 | 54         | 45                 |
| 53  | 33   | 20         | 12                 | 11                 | 57         | 45                 |
| 38  | 34   | 04         | 12                 | 80                 | 42         | 35                 |
| 35  | 14   | 21         | 18                 | 75                 | 40         | 40                 |
| 40  | 26   | 14         | 14                 | 65                 | 25         | 40                 |
| 36  | 33   | 03         | 16                 | 85                 | 49         | 35                 |
| $\bar{x}$ 36  |  | 15         | 15                 |                    | 53         | 58                 |
| SD 0.89   |  | 0.74       | 6.5                |                    | 2.74       | 19.7               |

poorer the flow in the leg examined, the later did it reach its minimum, but it was always lowest 3 to 4 seconds after the contrast medium had appeared in the main arteries and branches in the segment surrounded by the strain-gauge (Fig. 5)

On simultaneous measurements of the flow in a healthy and in a diseased leg of the same patient, the fall in flow to a minimum occurred earlier in the healthy

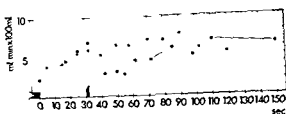


Fig. 8 (above) Blood flow during reactive hyperemia in leg with arterial obliteration. Examination performed without (\*) and with (•) angiography

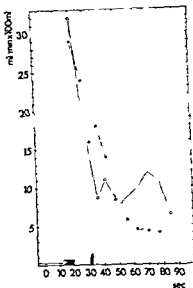


Fig. 9 (right) Blood flow during reactive hyperemia at angiography (○) and on injection of normal saline (\*) in a normal leg

Symbols as in fig. 6

Four measurements were made, always with the same result. No difference was recorded when the contrast medium was replaced by 5 % saline, which has approximately the same osmotic pressure. The effect on peripheral pressure and flow in the leg was also investigated after an injection of 5 % saline during reactive hyperemia, 5 seconds after this injection the flow was markedly reduced, with the same effect as that produced by contrast medium injection during reactive hyperemia.

The blood pressure in the vascular area where 5 % saline had been injected changed synchronously with the central blood pressure after the initial fall in pressure following the release of arterial occlusion. Measurements of pressure and flow after the respective injections of contrast medium and 5 % saline thus produced the same changes. The fall in pressure occurred both during rest and during reactive hyperemia. Both injection of contrast medium and 5 % saline produced a sensation of burning pain in the lower part of the back.

### Discussion

Injection of contrast medium into the lower part of the abdominal aorta was immediately followed by a flow reduction in the calf, which, when the femoral vessels were normal, was observed over a period of about 10 seconds and was followed by a marked increase in flow. These findings are in agreement with observations made on experiments in animals by MARSHALL & SHEPHERD (1959).

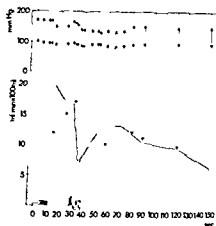


Fig 7 Central blood pressure and blood flow in a sound leg (○) and in a leg with arterial obliteration (●) at angiography during reactive hyperemia. Symbols as in fig 6.

*Flow in limbs with obliterated arteries* The effect of contrast medium in legs with arterial obliteration is given in Figs 7 and 8. The rising flow curve was interrupted 5 to 15 seconds after injection and the flow was minimal 15 to 20 seconds later. The flow again increased later and 60 to 70 seconds after the injection had reached a new maximum following hyperemia produced by the injection of the contrast medium. The degree of flow reduction appeared to vary with the severity of the arterial insufficiency.

*Measurement of peripheral pressure and flow on injection of contrast medium and injection of normal and 5% saline* Measurements of flow were also made when normal saline was injected in place of contrast medium, in order to determine whether the effect of the contrast medium was secondary to the increase in pressure during the injection. Figs 9 and 10 show the flow after the injection of saline and contrast medium respectively in normal legs and in legs with obliterated arteries. The flow in the leg following injection of saline was roughly the same as in the arm when angiography of the leg was performed.

In one patient with arterial obliteration at the level of the ankle, but with otherwise normal vessels, the effect of the contrast medium injection on the pressure and flow peripherally during rest was studied. The central blood pressure was recorded simultaneously (Fig 11). The blood pressure in the vascular area peripheral to the contrast bolus fell synchronously with the central blood pressure. The pressure was lowest 7 to 8 seconds after the occurrence of minimal flow and 8 to 9 seconds after the bolus had passed the measurement point in the middle of the thigh. The curve representing the pressure in the leg indicated a second fall later on because of the increased flow due to the hyperemia produced by the injected contrast medium. The central pressure was but little affected during the latter period.

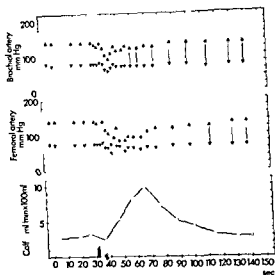


Fig 11 Blood flow during angiography of normal leg. The central blood pressure (brachial artery) and the peripheral blood pressure in the femoral artery of the leg were studied by arteriography. Symbols as in fig 6.

of the contrast medium, or increased viscosity of the blood due to aggregation, caused an instantaneous fall in blood pressure in the peripheral arteries of the leg. An instantaneous increase in viscosity of the blood in the lower part of the abdominal aorta and iliac arteries may, however, according to the law of Poiseuille, result in a decrease in flow through the calf, without any change in the peripheral blood pressure.

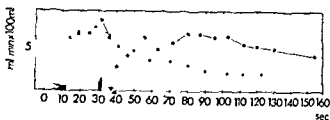
That the changes in flow are due to the increased viscosity of the blood is also supported by the finding that the lowest flow value occurred at the time when the contrast medium passed into the capillaries. Thus, in the presence of reactive hyperemia, the reduction occurred sooner because of the shortened circulation time and was more marked than during rest. For the same reason it occurred later and was more marked in patients with atherosclerosis.

The reduction in flow observed in the present investigation has practical consequences for the proper interpretation and performance of arteriography of the leg; it occurs during the period when contrast medium is passing through the arteries, i.e. during the informative period of examination. The marked delay in the passage of the contrast medium in obliterative disease, which is stressed by the hemodynamic effect of the medium, makes correct timing of the exposures still more difficult. Also, after reactive hyperemia, the contrast medium will reduce the flow markedly but not to the same low values as in resting conditions. Arteriography is therefore as a rule more informative when performed after reactive hyperemia.



Fig 10 Blood flow during reactive hyperemia at angiography (●) and on injection of normal saline (\*) in leg with arterial obliteration

Symbols as in fig 6



and SAKO (1963). The decrease in flow occurred before the contrast medium had reached the site where the flow was measured in the calf

The changes recorded in the blood flow after injection of a contrast medium may be due to changes in blood pressure, vascular tone and viscosity of the blood

**Blood pressure** Increase in the central blood pressure occurred during the injection of contrast medium, and a few seconds afterwards. The peripheral blood pressure in the arm and in the area examined with angiography followed the central pressure. In the arm, the increase in blood pressure was accompanied by a brief increase in flow. In the leg, the blood flow after the injection decreased initially and later on increased markedly. The increase in the blood flow in the leg was accompanied by a fall in the general blood pressure, with a decrease in the blood flow through the arm as a result. The blood flow through the arm, which was not directly influenced by the contrast medium, varied with the general blood pressure. The flow in the arm thus behaved differently from that in the legs following the intraarterial injection of contrast medium into the distal part of the lumbar aorta. This must mean that the changes in flow in the leg following an injection of contrast medium cannot be due to changes in the blood pressure.

**Vascular tone** It might be assumed that the brief reduction in flow following injection of contrast medium could be due to a change in vascular tone. Such a change, induced centrally via baroreceptors, appears less likely, however, because the arm flow and the leg flow were different. It might however be ascribed to a local reflex response, and perhaps correlated to the burning pain observed during the injection, because the reduction in flow occurred instantaneously at the beginning of the injection.

**Viscosity** It was thought that the high viscosity of the contrast medium, possibly increased still more by aggregation of blood cells, could have a plugging effect, resulting in a fall in blood pressure distal to the plug and thereby an instantaneous reduction in flow. The peripheral pressure measurements showed however that this could not be the case. Moreover, the same reduction in flow occurred following injection of 5 % saline, which has a lower viscosity than the contrast medium. We were thus unable to produce any evidence that the viscosity



## SUMMARY

Plethysmographic measurement of blood flow of the calf was performed during femoral arteriography of 25 legs in 15 patients. Simultaneous recording of the central blood pressure was made in nine of the patients. Instantaneous reduction in flow occurred in all legs after the contrast medium injection. The practical significance of the findings in the interpretation and performance of arteriography of the leg is discussed.

## ZUSAMMENFASSUNG

Plethysmographische Messung des Blutflusses wurde in der Wade während Femoralisangiographie von 25 Beinen in 15 Patienten vorgenommen. Gleichzeitig wurden Bestimmungen des zentralen Blutdruckes in neun Patienten durchgeführt. Eine unmittelbare Reduktion des Blutzuflusses zur Wade erfolgte nach der Injektion von Kontrastmittel. Die praktische Bedeutung dieser Befunde wird erörtert.

## RÉSUMÉ

Les auteurs ont fait des mesures plethysmographiques du débit sanguin dans le mollet au cours de l'arteriographie femorale de 25 membres inférieurs chez 15 malades. Ils ont enregistré simultanément la pression sanguine centrale chez neuf de ces malades. Dans tous les membres inférieurs le débit est instantanément réduit après l'injection du moyen de contraste. Les auteurs examinent l'intérêt pratique de ces résultats pour l'interprétation et l'exécution de l'arteriographie du membre inférieur.

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Table 1

*Effect on the protein bound iodine (PBI) and the butanol-extractable iodine (BEI) of additions in vitro of large amounts of different contrast media to serum*

|                       | Iodine added<br>μg iodine/l | PBI μg/l | BEI μg/l |
|-----------------------|-----------------------------|----------|----------|
| Serum before addition | —                           | 52       | 41       |
| Urografin 60 %        | 2 890                       | > 400    | 44       |
| Gastrografin          | 2 140                       | 386      | 35       |
| Conray 300            | 2 790                       | > 400    | 50       |
| Isopaque 45 %         | 770                         | > 400    | 42       |
| Periodal H viscous    | 2 940                       | > 400    | 330      |
| Biligradin forte      | 2 400                       | > 400    | 70       |
| Bilivistan            | 2 580                       | > 400    | 38       |
| Biloptin              | 1 660                       | > 400    | > 400    |
| Kontrast U (Leo)      | 1 120                       | 208      | 41       |
| Dionosil              | 790                         | > 400    | 125      |

Table 2

*Effect on the protein bound (PBI) and the butanol extractable iodine (BEI) of additions in vitro of different contrast media to serum — The amounts added were ten times smaller than those in table 1*

|                       | Iodine added<br>μg/iodine/l | PBI μg/l | BEI μg/l |
|-----------------------|-----------------------------|----------|----------|
| Serum before addition | —                           | 52       | 41       |
| Urografin 60 %        | 289                         | 111      | 42       |
| Gastrografin          | 214                         | 88       | 44       |
| Conray 300            | 279                         | 138      | 45       |
| Isopaque 45 %         | 77                          | 72       | 45       |
| Periodal H viscous    | 294                         | 77       | 68       |
| Biligradin forte      | 240                         | 266      | 51       |
| Bilivistan            | 258                         | 266      | 44       |
| Biloptin              | 166                         | 153      | 142      |
| Kontrast U (Leo)      | 112                         | 60       | 38       |
| Dionosil              | 79                          | 80       | 61       |

The total amount of iodine in the extracellular space is small, only about 0.5 mg, and it is therefore natural that the plasma iodine level will be influenced by exogenously added iodine. An amount of 1800 mg of iodine, for instance, is added in cholecystography, and this means an enormous increase of the iodine concentration in the plasma.

## EFFECT OF IODINATED ROENTGENOGRAPHIC CONTRAST MEDIA ON BUTANOL-EXTRACTABLE, PROTEIN-BOUND, AND TOTAL IODINE IN SERUM

by

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The iodine determination in serum, usually by analysis of protein bound iodine, is an important method for investigation of the thyroid function. The iodine levels in hypothyroidism are usually decreased while elevated values are encountered in hyperthyroidism. The dominating iodine compound in serum is thyroxine, which may be determined quantitatively by analysis of the butanol extractable iodine. A small amount of triiodothyronine is usually also present. Protein bound iodine is also dominated by thyroxine, but in addition to triiodothyronine, iodinated albumin and, according to which method of analysis is used, also small quantities of monoiodotyrosine and diiodotyrosine may be found. The values of the latter may be considerably elevated in pathologic conditions. Also thyroglobulin may, sometimes occur in the plasma, it elevates the protein bound iodine level but has no effect on the butanol extractable iodine. The total iodine contents consist not only of the iodine compounds included in the protein bound iodine but above all the iodides as well.

Table 4

*In two determinations of total iodine, protein bound iodine (PBI) and butanol-extractable iodine (BEI) before and after injections of Urografin for urography — The amount of iodine injected was in all cases 11.6 g except for Case 12 in which the amount was 8.7 g*

| Case No | Level before injection |     |     | Level 7 days after injection |     |     | Level 30 days after injection |     |     |
|---------|------------------------|-----|-----|------------------------------|-----|-----|-------------------------------|-----|-----|
|         | Total                  | PBI | BEI | Total                        | PBI | BEI | Total                         | PBI | BEI |
| 1       | 60                     | 58  | 56  | 67                           | 63  | 42  | 64                            | 64  | 37  |
| 2       | 73                     | 61  | 53  | 30.6                         | 96  | 52  | 69                            | 56  | 50  |
| 3       | 50                     | 47  | 50  | 50                           | 48  | 46  | 54                            | 42  | 40  |
| 4       | 63                     | 50  | 42  | 50                           | 44  | 31  | 59                            | 53  | 50  |
| 5       | 54                     | 49  | 38  | 57                           | 55  | 51  | 67                            | 51  | 50  |
| 6       | 39                     | 36  | 29  | 49                           | 47  | 42  | 53                            | 44  | 40  |
| 7       | 61                     | 53  | 41  | 57                           | 50  | 41  | 57                            | 50  | 47  |
| 8       | 59                     | 56  | 47  | 51                           | 48  | 44  | 50                            | 40  | 37  |
| 9       | 61                     | 55  | 37  | 78                           | 76  | 42  | 04                            | 53  | 44  |
| 10      | 60                     | 52  | 40  | 40                           | 43  | 39  | 49                            | 42  | 36  |
| 11      | 50                     | 46  | 40  | 52                           | 45  | 41  | 46                            | 38  | 38  |
| 12      | 40                     | 38  | 31  | 52                           | 30  | 24  | 47                            | 43  | 39  |
| 13      | 61                     | 49  | 43  | 55                           | 49  | 38  | 55                            | 46  | 44  |
| 14      | 62                     | 67  | 44  | 56                           | 52  | 40  | 06                            | 53  | 41  |
| 15      | 57                     | 56  | 45  | 58                           | 54  | 52  | 62                            | 53  | 46  |
| 16      | 62                     | 62  | 42  | 60                           | 51  | 42  | 97                            | 54  | 42  |
| 17      | 88                     | 70  | 42  | 65                           | 56  | 48  | 88                            | 54  | 41  |
| 18      | 57                     | 57  | 40  | 58                           | 42  | 34  | 42                            | 38  | 33  |
| 19      | 40                     | 40  | 37  | 48                           | 45  | 37  | 46                            | 45  | 38  |

Serum from patients referred for urography, cholecystography or cholangiography were analyzed for total iodine, protein bound iodine and butanol extractable iodine before the contrast medium was administered, as well as at 7 and 30 days afterwards. The contrast media used in these studies were iothalamine (Conray), sodium diatrizoate (Urografin and Urovison), diiodoatophan (Biloptin), and ioglycamic acid (Bilvistan). The injected amounts of iodine with the different contrast media are recorded in Tables 3 to 6. The patients who underwent lymphography received 10.4 g of iodine in the form of Lipiodol, which is an iodized poppy seed oil.

*Methods.* Iodine analyses were carried out by the Jacobsson method, after wet ashing (Zak et coll.) and colorimetric determination by a modified form of the Sandell Kolthoff method. Gel filtration was used for isolation of the protein-bound iodine (JACOBSSON & WIDSTROM). Duplicate determinations were made

Table 3

*In vivo* determinations of total iodine, protein bound iodine (PBI) and butanol-extractable iodine (BEI) before and after injections of Conray and Urovison for urography

| Case No | Medium and gram iodine injected | Levels before injection |     |     | Levels 7 days after injection |     |     | Levels 30 days after injection |     |     |
|---------|---------------------------------|-------------------------|-----|-----|-------------------------------|-----|-----|--------------------------------|-----|-----|
|         |                                 | Total                   | PBI | BEI | Total                         | PBI | BEI | Total                          | PBI | BEI |
| 1       | Conray 8 g                      | 110                     | 110 | 92  | 133                           | 130 | 91  | 102                            | 98  | 88  |
| 2       |                                 | 55                      | 44  | 44  | 56                            | 54  | 40  | 48                             | 41  | 39  |
| 3       |                                 | 54                      | 54  | 49  | 64                            | 64  | 43  | 57                             | 54  | 53  |
| 4       |                                 | 57                      | 54  | 48  | 66                            | 64  | 59  | 67                             | 66  | 40  |
| 5       | Urovison 81 g                   | —                       | 69  | 45  | 88                            | 79  | 45  | 68                             | 55  | 45  |
| 6       |                                 | 47                      | 44  | 39  | 61                            | 41  | 38  | 42                             | 35  | 34  |
| 7       |                                 | 61                      | 56  | 43  | 49                            | 47  | 46  | 52                             | 49  | 39  |

These factors are of considerable significance in iodine analyses. Apart from the amounts of added iodine, the chemical properties and elimination speed of the iodinated contrast media, as well as the technique used for the analysis, all play a part in the final result of the iodine determination.

The effect of iodine-containing contrast media for roentgenographic purposes was investigated both *in vitro*, by adding different concentrations to serum in order to ascertain how the butanol-extractable iodine and protein bound iodine are influenced, and *in vivo*. In the latter investigations the total iodine level was also determined. Iodine determinations were carried out before, as well as at different times after, the administration of the medium in connection with urography, oral cholecystography, and intravenous cholegraphy. The iodine levels were also determined after lymphography with Lipiodol, because of the slow elimination speed of this contrast medium.

*Material* Iodinated roentgenographic contrast media in amounts corresponding to an iodine content of 400 to 2890  $\mu\text{g/l}$  serum (Table 1) and to a ten times lower concentration (40 to 289  $\mu\text{g/l}$  serum) (Table 2) were added to serum in which protein-bound iodine and butanol-extractable iodine determinations had been made. The following contrast media were used: sodium diatrizoate (Urografin, Gastrografin), iothalamine (Conray), sodium metrizoate (Isopaque), iodoxypyracet (Periodal H viscous), ioglucamic acid (Bilivistan), adipiodone (Biligrafin forte), diiodoatophan (Biloptin), methiodal (Kontrast U) and propylidone (Dionosil). Determinations of protein-bound iodine and of butanol extractable iodine were made in these sera.

Table 6

*In vivo determinations of total iodine, protein bound iodine (PBI) and butanol-extractable iodine (BEI) before and after administration of Biloptin (1.8 g per os iodine injected) for peroral cholecystography*

| Case No | Level before administration |     |     | Level 7 days after administration |       |       | Level 30 days after administration |       |     |
|---------|-----------------------------|-----|-----|-----------------------------------|-------|-------|------------------------------------|-------|-----|
|         | Total                       | PBI | BEI | Total                             | PBI   | BEI   | Total                              | PBI   | BEI |
| 1       | —                           | —   | —   | > 400                             | > 400 | > 400 | > 400                              | > 400 | 53  |
| 2       | —                           | —   | —   | > 400                             | > 400 | > 400 | > 400                              | > 400 | 49  |
| 3       | —                           | —   | —   | > 400                             | > 400 | > 400 | > 400                              | > 400 | 56  |
| 4       | 89                          | 64  | 60  | > 400                             | > 400 | > 400 | > 400                              | > 400 | 72  |
| 5       | 87                          | 72  | 66  | > 400                             | > 400 | > 400 | > 400                              | 356   | 115 |
| 6       | 46                          | 43  | 37  | > 400                             | > 400 | 101   | 335                                | 298   | 47  |
| 7       | 79                          | 76  | 66  | > 400                             | > 400 | 237   | 391                                | 362   | 94  |
| 8       | 70                          | 62  | 54  | 392                               | 358   | 248   | 303                                | 255   | 83  |
| 9       | 60                          | 60  | 41  | > 400                             | > 400 | 351   | 380                                | 358   | 52  |
| 10      | 51                          | 38  | 37  | > 400                             | 323   | 249   | > 400                              | 259   | 71  |
| 11      | 50                          | 45  | 45  | > 400                             | > 400 | 351   | > 400                              | 382   | 61  |

Urografin, administered intravenously (Table 4), had no appreciable effect on the butanol extractable iodine, protein-bound iodine and total iodine values, except in one instance (Case 2) in which the protein-bound iodine was considerably, and the total iodine grossly elevated. After administration of the contrast iodine levels, protein bound iodine levels returned to the initial value.

After intravenous administration of Bilivistan (Table 5) the butanol extractable iodine level was in seven cases out of eight higher than the initial value at seven days, but the upper normal limit was exceeded in only four of these cases. All the butanol extractable iodine values returned to normal in thirty days. The total iodine and the protein bound iodine were considerably to grossly elevated at seven days, at thirty days they had decreased considerably but were still above the normal range. An appreciable difference was noted between values of the total iodine and protein bound iodine on the one hand and the butanol-extractable iodine on the other.

After peroral administration of Biloptin (Table 6) the butanol extractable iodine levels at seven days were considerably to grossly elevated. The values returned to the normal range within thirty days in six of eleven cases, while in the others the values were still elevated but lay within the physiologic limits.

All the protein-bound iodine and total iodine values exceeded the physiologic



Table 5

*In vivo determinations of total iodine, protein-bound iodine (PBI) and butanol extractable iodine (BEI) before and after injections of Bilivistan (5.5 g iodine injected) for intravenous cholangiography*

| Case No | Level before injection |     |     | Level 7 days after injection |     |     | Level 30 days after injection |     |     |
|---------|------------------------|-----|-----|------------------------------|-----|-----|-------------------------------|-----|-----|
|         | Total                  | PBI | BEI | Total                        | PBI | BEI | Total                         | PBI | BEI |
| 1       | 54                     | 52  | 41  | 172                          | 161 | 63  | 96                            | 95  | 59  |
| 2       | 79                     | 68  | 63  | 204                          | 192 | 73  | 127                           | 113 | 65  |
| 3       | 49                     | 46  | 35  | 365                          | 288 | 83  | 137                           | 135 | 53  |
| 4       | 52                     | 52  | 40  | 335                          | 313 | 68  | 100                           | 84  | 26  |
| 5       | 48                     | 46  | 26  | > 400                        | 396 | 45  | 97                            | 94  | 51  |
| 6       | 43                     | 41  | 36  | 270                          | 251 | 49  | 132                           | 128 | 48  |
| 7       | 50                     | 49  | 45  | 185                          | 158 | 66  | 96                            | 86  | 46  |
| 8       | 64                     | 63  | 50  | 214                          | 176 | 50  | 115                           | 109 | 58  |

in all cases. The normal values per liter of serum are 32 to 65  $\mu$ g for butanol-extractable iodine, 35 to 75  $\mu$ g for protein-bound iodine, and 37 to 88  $\mu$ g for total iodine. The exact value was not determined in iodine concentrations greatly exceeding the physiologic range but the level is given.

## Results

As may be seen from Table 1, no definite increase in the *in vitro* butanol-extractable iodine level was obtained for seven of the eleven tested contrast media. Of the other four media Biligrafin forte caused a slight increase and Dionosil a moderate increase, while Perjodal H and Biloptin gave values far above the physiologic range.

All the media investigated caused an elevation in the protein-bound iodine level, and except in the case of Kontrast U the values were grossly elevated.

The tendency was the same, although of a lower degree, after addition of a ten times smaller amount of contrast medium (cf. Table 2). Expressed as a percentage of added iodine the protein-bound iodine elevation was 89%, 83%, and 61% for Biligrafin forte, Bilivistan, and Biloptin, respectively, and much lower for Urografin (20%), Gastrografin (17%), Conray (31%), and Isopaque (26%). The lowest increase was noted with Perjodal H (9%) and Kontrast U (7%).

Intravenous injection of Conray did not influence the butanol extractable iodine and total iodine values. Similar results were obtained with Urovison.

present results Cholegraphy caused a slight elevation of the butanol extractable iodine. Dionosil produced gross elevation of the butanol extractable iodine level, whereas a moderate increase was observed in the present study. Variations in the protein binding, and the definite risk of contamination that always exists in work with high iodine concentrations, may explain the discrepancy. The contrast media studied were in other respects not directly comparable, but certain urographic media and other allied substances caused an insignificant or no elevation at all in the butanol extractable iodine values while oral cholecystographic media gave grossly elevated levels. This agrees with the present observations. Thus, with the exceptions mentioned above, the butanol extractable iodine, as opposed to the protein bound iodine, gave a correct value for the hormonal iodine level after the addition of iodinated contrast media.

The distribution between protein bound and non protein bound contrast media could be determined from the elevation of the protein bound iodine expressed as a percentage of the amount of added iodine. The gallbladder contrast medium lay in this respect at a considerably higher level than the corresponding value for the urographic media.

Of the contrast media studied *in vivo* the elimination times were short for Conray, Urografin and Urovison, of medium duration for Bilivistan, long for Biloptin and very long for Lipiodol. No increase in the butanol extractable iodine value was observed after *in vivo* administration of the urographic contrast media Conray, Urografin and Urovison. This accords with the findings of other investigators (FRISCHAUFF *et coll*, PILEGGI *et coll*). Nor was there any effect on the protein bound iodine and total iodine after seven days (cf. OGDEN & SHELINE, THOREN, FOLDENAUER *et coll*) except in one case in which the protein bound iodine was considerably increased and the total iodine concentration grossly increased. Impaired renal function had probably delayed the elimination (Table 4, Case 2).

The large difference between the total iodine and protein bound iodine is an indication that the balance between free and protein bound Urografin has been displaced in the direction of the free form. This explains the rapid elimination in connection with normal renal function. The values were normal thirty days after the injection. To obtain a correct value for the hormonal iodine level, a determination of the butanol extractable iodine was therefore necessary.

TALROG & CHAIKOFF reported that cholecystographic contrast media gave elevated butanol extractable iodine values. Bilivistan in the present material interfered mainly with the total iodine and the protein bound iodine *in vivo* but a certain effect on the butanol extractable iodine was noted after seven days. At thirty days, however, the butanol extractable iodine had returned to normal. HONETZ & KOTZAUER obtained grossly elevated values during the first six days

Table 7

*In vivo determinations of total iodine, protein bound iodine (PBI) and butanol extractable iodine (BEI) after injection of Lipiodol for lymphography*

| Case No | Interval in days between injection and sampling | Total iodine | PBI   | BEI |
|---------|---|--------------|-------|-----|
| 1       | 261   | 227          | 165   | 54  |
| 2       | 42  | > 300        | > 300 | 184 |
| 3       | 69  | > 300        | > 300 | 159 |
| 4       | 353   | 140          | 130   | 61  |
| 5       | 325   | 180          | 132   | 67  |

limit seven days after the administration. At thirty days, only three cases lay within this range but the levels were still grossly elevated as compared with the initial values. There was a marked difference between the total iodine and protein-bound iodine on the one hand and the butanol-extractable iodine on the other.

The results from patients given Lipiodol at lymphography are shown in Table 7. The butanol-extractable iodine values lay within or close to the normal range in the three cases where the longest time had elapsed between injection and sampling (261, 325 and 353 days). The total iodine and protein-bound iodine values were considerably elevated but lay within the physiologic range. In the other two cases, in which the specimens had been taken 42 and 69 days, respectively, after administration of the contrast medium, the butanol extractable iodine levels were considerably elevated and the total iodine and protein-bound iodine were above the physiologic range. There was an appreciable difference between the total iodine and protein-bound iodine in comparison with the butanol-extractable iodine values.

### Discussion

This investigation of the effect of *in vitro* additions of iodinated contrast media has indicated that the butanol-extractable iodine, unlike the protein-bound iodine, was not usually affected. Biloptin and Perjodal, and to a lesser degree Diosonil and Biligrafin forte, formed exceptions.

Similar studies were carried out by PILEGGI *et coll.*, who added *in vitro* 1000  $\mu$ g of iodine in the form of different contrast media. Regarding the amount added, this would correspond to the series with the higher iodine additions in the present investigation. Elevated protein bound iodine values were obtained with all the contrast media tested, an observation entirely in agreement with the

of these 1000 sera on the other hand, only the total iodine and the protein bound iodine values were elevated, while the butanol extractable iodine was within normal range. The determination of butanol extractable iodine is thus the most reliable of the three methods for assessment of the thyroid function.

It is obvious from the above however that some roentgenographic contrast media also may cause elevation of the butanol extractable iodine level, and the use of this method may produce misleading results. When there is a marked increase to levels above the physiologic range, the situation is obvious, however, and there is practically no risk that an incorrect evaluation will be made. The high value in these cases can be explained by the exogenously added iodine. The interpretation will however be more difficult when sera with a moderate increase not exceeding the physiologic limit are to be evaluated. In such cases, a total iodine and protein bound iodine determination concurrently with the butanol extractable iodine analysis will often reveal the presence of exogenous iodine, since the difference between the butanol extractable iodine on the one hand and the total iodine and protein bound iodine on the other hand is usually greater than in physiologic conditions. It would appear therefore that butanol-extractable iodine and hormonal iodine determinations should always be combined with an analysis of the protein bound iodine and the total iodine.

## SUMMARY

Butanol extractable iodine and protein bound iodine determinations were made in serum to which different amounts of iodinated contrast media had been added. The butanol-extractable iodine, protein bound iodine and total iodine were also measured in serum from patients given iodinated contrast media with different elimination speeds. The value of the methods for the estimation of thyroid function after administration of various contrast media is discussed.

## ZUSAMMENFASSUNG

Das proteingebundene und Butanol extrahierte Jod wurde im Blutserum zu dem wechselnden Betrage von jodhaltigen Kontrastmitteln zugesetzt und quantitativ bestimmt. Das Butanol extrahierte, proteingebundene und totale Jod wurde auch im Serum von Patienten nach vorheriger Injektion jodhaltiger Kontrastmittel verschiedener Ausscheidungsgeschwindigkeiten gemessen. Der Wert der Methoden für die Bestimmung der Schilddrüsenfunktion nach Verabreichung verschiedener Kontrastmittel wird diskutiert.

## RÉSUMÉ

Les auteurs ont dosé l'iode extractible par le butanol et l'iode protéique dans du serum auquel avait été ajoutés des moyens de contraste iodés en différentes proportions. Ils ont aussi dosé l'iode extractible par le butanol, l'iode protéique et l'iode total.

with Biloptin, an observation that tallies well with the results at seven days in the present investigation. Because of the slow elimination, five out of eleven butanol-extractable iodine values were still moderately increased thirty days after administration but were well within the physiologic range. In the other cases, the butanol-extractable iodine had returned to normal. Compared with the protein-bound iodine and total iodine, the butanol-extractable iodine became normal much more rapidly. The protein-bound iodine cannot be expected to reach the initial level until after three to four months (HOVETZ & KOTZAREK, GOLDENAUER et coll.).

The elimination of Lipiodol depends on the mode of administration (THORÉN). Intratracheal administration causes an elevation of the protein-bound iodine lasting for one to two years (MAN & PETERS, HEIJDEMAN & LINDEBOOM). In the present cases also, there was a prolonged elevation of total iodine and protein-bound iodine after lymphography, whereas the butanol-extractable iodine was again normal at 261 to 353 days.

Thus, neither the butanol-extractable nor the protein-bound iodine and the total iodine were affected by contrast media with a short elimination time and a relatively low degree of protein binding (Conray, Urografin, Urovison). A contrast medium with an elimination time of moderate duration (Bilvistin) had a slight effect on the former, thirty days after the administration; however, the values were within the normal range. The protein-bound iodine and the total iodine were considerably to grossly elevated and were of the same magnitude. There was a characteristic difference in level between the total iodine and the protein-bound iodine on the one hand and the butanol-extractable iodine on the other.

When a contrast medium with a long elimination time was given (Biloptin), normalization of the butanol-extractable iodine occurred first, while the protein-bound and total iodine levels were still very high and of the same magnitude. A contrast medium with a very long elimination time (Lipiodol) had a marked effect on the butanol-extractable as well as on the protein-bound and the total iodine, but the butanol-extractable iodine level became normal much more rapidly.

Iodinated drugs and contrast media are being used so extensively today that iodine determinations in serum increasingly often give misleading information regarding the thyroid function. Contrast media seem to play a significant part in such results (JACOBSSON).

In an analysis of just over 1000 consecutive sera at the Central Chemical Laboratory at Umeå it was found that 0.8% had grossly elevated total iodine, protein-bound and butanol-extractable iodine values exceeding the physiologic limit. These analyses were thus worthless from the clinical standpoint. In 4%

of these 1000 sera on the other hand, only the total iodine and the protein bound iodine values were elevated, while the butanol extractable iodine was within normal range. The determination of butanol extractable iodine is thus the most reliable of the three methods for assessment of the thyroid function.

It is obvious from the above however that some roentgenographic contrast media also may cause elevation of the butanol extractable iodine level, and the use of this method may produce misleading results. When there is a marked increase to levels above the physiologic range, the situation is obvious, however, and there is practically no risk that an incorrect evaluation will be made. The high value in these cases can be explained by the exogenously added iodine. The interpretation will however be more difficult when sera with a moderate increase not exceeding the physiologic limit are to be evaluated. In such cases, a total iodine and protein bound iodine determination concurrently with the butanol extractable iodine analysis will often reveal the presence of exogenous iodine, since the difference between the butanol extractable iodine on the one hand and the total iodine and protein-bound iodine on the other hand is usually greater than in physiologic conditions. It would appear therefore that butanol-extractable iodine and hormonal iodine determinations should always be combined with an analysis of the protein bound iodine and the total iodine.

## SUMMARY

Butanol extractable iodine and protein-bound iodine determinations were made in serum to evaluate thyroid function after administration of various contrast media is discussed.

## ZUSAMMENFASSUNG

Das proteingebundene und Butanol extrahierte Jod wurde in Blutserum zu dem wechseln de Betrage von jodhaltigen Kontrastmitteln zugefugt wurden quantitativ bestimmt. Das Butanol extrahierte proteingebundene und totale Jod wurde auch im Serum von Patienten nach vorheriger Injektion jodhaltiger Kontrastmittel verschiedener Ausscheidungsgeschwindigkeiten gemessen. Der Wert der Methoden fur die Bestimmung der Schilddrusenfunktion nach Verabreichung verschiedener Kontrastmittel wird diskutiert.

## RÉSUMÉ

Les auteurs ont dosé l'iode extractible par le butanol et l'iode protéique dans le sérum auquel avait été ajoutées des quantités variables de produits de contraste iodés. Ils ont aussi dosé l'iode extractible et l'iode protéique dans le sérum de malades qui avaient reçu des produits de contraste iodés. Ils examinent la valeur des méthodes pour l'évaluation de la fonction thyroïdienne après l'administration de diffé-

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## MICTURITION URETHROCYSTOGRAPHY IN CHILDREN WITH MYELOMENINGOCELE

A radiologic and clinical investigation

by

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The purpose of the present paper is to describe the urethrocystographic findings in children with myelomeningocele and to endeavour to correlate the variations observed with certain clinical variables such as neurologic changes, the incidence of urinary tract infections residual urine volumes, and different patient ages. The material includes two patients with adequate bladder function and unilateral neurologic functional defects who have already been described in an earlier report (ERICSSON *et coll* 1970a). The clinical parameters having significance as continence promoting factors, both as regards bladder and anal function, have been analyzed in another investigation (ERICSSON *et coll* 1970b), also based on the present material.

Recent investigations (COOPER 1968, STARK 1968, and others) of bladder functions with electromanometric pressure flow measurements and electromyographic recordings in cases of myelomeningocele, have demonstrated that detrusor function and the activity of the striated muscle of the sphincter and pelvic floor

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may vary considerably. It thus seems likely that variations may also occur in the urethrocytograms. A better knowledge of neurogenic bladder dysfunction is needed before more rational therapeutic measures can be applied.

*Material and Methods* The case material consists of 23 boys and 27 girls referred for urologic investigation during the years 1962 to 1966. Most of them were under observation for several years, and in general those who were followed up had received hospital care once or twice a year, some had been observed since the neonatal period. At the time of the latest examination, the ages varied from 2 to 16 years. The residual urine was determined repeatedly after spontaneous micturition or Credé's manoeuvre. Roentgen examination with excretion urography and micturition urethrocytography was carried out in 48 cases (21 boys and 27 girls).

*Roentgen examinations* The number of examinations with excretion urography and micturition urethrocytography varied from 1 to 8 per case. Compression was applied over the ureters at the first examination at urography of children aged over 3 to 6 months. Films of the kidneys as well as of the entire urinary tract, including the bladder, were obtained, at the control examinations, the procedure was often simplified, the compression of the ureters being omitted and the number of exposures reduced. Efforts were made to achieve optimal contrast filling of the renal pelvis and ureters.

Micturition urethrocytography was carried out separately, and never immediately following urography, it was usually done on the following day. Most cases were examined supine (RUDHE 1964). The contrast medium was pressed into the bladder through a plastic catheter inserted via the urethra. Sterile barium emulsion was used in the earlier stages of the investigations (HJELLBERG et coll. 1957) but this has been replaced to an increasing extent by a water soluble contrast medium (Isopaque-Cysto, Nyegaard). During micturition, the films were exposed consistently in a p and lateral projections as well as in a modified a p projection with the central ray from the overcouch tube directed 15 to 20° cranially. Oblique views were also taken when necessary. In addition films were obtained during bladder filling and after completed micturition or an attempt at voiding. The examinations were performed without fluoroscopy, and retrograde urethrography was not employed in this series.

The roentgenologic evaluation of the findings in the urinary tract in the present series was made without any knowledge of the clinical urologic status, nor of the neurologic observations. Special emphasis was placed on assessment of the shape of the bladder, the presence of trabeculation and pseudo diverticula, signs of detrusor activity, reflux to the upper urinary tract, the appearances of the bladder neck at rest and during attempts at urination, the width of the

Table 1  
*Reflexes present below different levels of neurologic lesions*

| Level of neurologic lesion | Number of cases examined | Patellar reflexes preserved | Achilles tendon reflexes preserved | Plantar reflexes preserved | Ano cutaneous reflexes preserved | Babinski's sign positive |
|----------------------------|--------------------------|-----------------------------|------------------------------------|----------------------------|----------------------------------|--------------------------|
| Low thoracic               | 6                        | 2                           | 4                                  | 4                          | 3                                | 3                        |
| High lumbar                | 10                       | 0                           | 1                                  | 0                          | 3                                | 1                        |
| Low lumbar                 | 5                        |                             | 0                                  | 0                          | 2                                | 0                        |
| High sacral                | 22                       |                             | 1                                  | 5                          | 1                                | 2                        |
| Low sacral                 | 7                        |                             |                                    |                            | 0                                | 0                        |
| Total                      | 50                       | 2                           | 6                                  | 9                          | 9                                | 6                        |

urethra at the site of the external sphincter, the occurrence of hydronephrosis and hydro ureter, and occasionally the level of the pelvic floor as well. Several of these parameters were determined semi quantitatively. The effect of pudendal nerve anesthesia when carried out was assessed at additional roentgen examinations.

*Neurologic classification.* The cases were classified according to the level of the lesion on the basis of the extent of the defects in motor function and sensibility, as well as loss of reflexes. The occurrence of persisting functions caudal to the lesion level was also recorded.

*Group 1 Low thoracic.* Two main types were observed. The first had the character of a partial transverse spinal lesion with predominantly spastic features, the sensory loss varied, and the ano cutaneous reflex was preserved. The other type had extensive areas of paresis with total, flaccid paraplegia and sometimes also weakness of the trunk and abdominal muscles. There was usually total sensory loss in the same segment, or with the cranial limit slightly lower. No ano cutaneous reflex was recorded.

*Group 2 High lumbar.* Most of these cases had subtotal paraparesis, sometimes with slight function retained in the hip flexors and adductors. There was a sensory loss in the corresponding segment, or with the upper limit slightly lower, a total loss of reflexes in the lower limbs was usually observed. Cases that partly resembled a partial spinal lesion with signs of mild spasticity or preserved ano cutaneous reflex activity, or both, were also encountered.

*Group 3 Low lumbar.* The hip flexors, hip adductors, and knee extensors were largely unimpaired. There was a sensory loss corresponding to the motor lesion level, or with the upper limit slightly lower. The patellar reflexes were

Table 2

*Infection index and residual urine volumes*

| Residual urine | Infection index |         |         |
|----------------|-----------------|---------|---------|
|                | 0-0.2           | 0.3-0.7 | 0.8-1.0 |
| 30 ml          | 3               | 2       | 2       |
| 30 to 100 ml   | 2               | 7       | 3       |
| 100 ml         | 0               | 2       | 10      |
| Total          | 5               | 11      | 15      |

preserved, although sometimes they were slightly less brisk. The Achilles tendon and plantar reflexes were absent, and there were no signs of spasticity. The ano-cutaneous reflex was preserved in 2 cases.

*Group 4 High sacral* The motor abnormalities included weakened function of the hip extensors and abductors, the knee flexors, and usually greatly reduced foot and toe motility as well. A sensory loss corresponding to the level of the motor lesion or with an upper limit slightly below it was observed. The Achilles tendon and plantar reflexes were absent. No signs of spasticity were noted. The ano-cutaneous reflex was preserved in one case.

*Group 5 Low sacral* No motor changes were recorded. A sensory loss corresponded to the lowest sacral segments. The Achilles tendon and plantar reflexes were preserved, but the ano-cutaneous reflex was always absent.

As the preservation of the reflex activity below the level of the lesion is of some significance in the discussion to follow, its incidence is presented in detail in Table 1. Isolated reflex function below the lesion level was thus commoner when the lesions were located at the higher levels. Regarding the ano-cutaneous reflex, it may be mentioned that it was present in 2 newborn infants, but disappeared later. Signs of spasticity in the form of ankle clonus and a positive Babinski reflex were sometimes noted.

*Clinical observations* The residual urine volume was in 12 cases consistently less than 30 ml, in 17 cases it was 30 to 100 ml on at least one occasion, and in 19 cases it amounted to over 100 ml at one or several recordings. There seemed to be no relation between the amount of residual urine and the level of the neurologic lesions although it appeared to be related to the patient's age. The mean age for the group with less than 30 ml was 5.5 years, whereas it was 10 years for the group with more than 100 ml residual urine volume.



FIG. 1. Micturition urethrocystograms. (a) Normal voiding pattern. (b) and (c) show a large, rounded bladder neck and upper part of posterior urethra.

A semi quantitative 'infection index' was calculated for the cases, 31 in all, that had been admitted to hospital at least three times at intervals of six months. The index indicates the number of times signs of urinary tract infection were present on admission in relation to the total number of admissions. Table 2 shows that the infection index increased with the residual urine volume. Approximately half the cases had an infection nearly every time they were in hospital. Girls seemed to be infected slightly more often than boys, 10 out of 17 girls belonged to the group with a high rate of infections as compared with 5 out of 14 boys. No definite relationship was established between the infection index and the level of the neurologic lesion.

*Roentgen observations.* Micturition urethrocystography revealed in the individual cases comparatively little change in the appearances from one examination to the subsequent one. A few exceptions to this rule were noted however. Thus, the cases observed over a long period not infrequently presented some progression of the roentgenologic changes, as for instance advancing dilatation of the upper urinary tract, or increasing trabeculation of the bladder. The significant abnormalities will be described separately.



Fig. 2 Bladder and urethra in myelomeningocele of the low thoracic flaccid type of cord lesion. Boy 2 years old. a) Excretion urography. Widely open funnel shaped bladder neck and patent posterior urethra closed by external sphincter below verumontanum. Bilateral hydronephrosis and abnormal appearances of bladder. b) c) Micturition urethrocytography. Elongated bladder which is top shaped, trabeculated and with multiple saccules. Diaphragmatic part of urethra is narrowed by external sphincter.

*Shape of the bladder.* A characteristic alteration in the bladder shape was observed almost consistently in 40 out of 48 cases (Figs 1, 2 and 3). The bladder was abnormally elongated and this abnormality sometimes seemed even greater when the upper part of the viscus was demarcated from the broader cranial part (Fig. 4), or the dome was pointed (Fig. 2). Not infrequently a partially patent urachus was demonstrated (Fig. 1). In a further 3 cases abnormal elongation of the bladder was an inconstant finding, and in 5 cases, the bladder had a normal appearance. The abnormal shape had no preference for any particular age; it was also observed in small children and infants, and there was no relationship to the level of the neurologic lesion or to the infection index.

*Trabeculation and pseudo-diverticula.* Trabeculation of the bladder wall was a constant finding in 28 cases, occurred inconstantly in 6 and developed gradually in 4 cases (Figs 2 and 3).

Increasing trabeculation was observed in 6 cases that had been followed up over a fairly long period. A higher frequency of trabeculation was noted among the cases with high lesion levels although no connection with the rate of occur-



Fig 3 Micturition urethrocytography in myelomeningocele of the high sacral type of cord lesion. Girl 4 years old. Elongated bladder of reduced capacity. Moderately increased trabeculation and scattered saccules and diverticula. Unilateral vesico-ureteral reflux, slightly widened bladder neck and urethra dilated above a constricting external sphincter.

rence or severity of urinary tract infection or sex of the patient was apparent. The 5 cases previously mentioned, with consistently normal-shaped bladders, had no signs of trabeculation. Trabeculation was confined to abnormally elongated bladders. The bladder was smooth-walled in 10 cases. Trabeculation was observed in all age groups. Pseudo-diverticula were common associated findings, especially when trabeculation was marked (Fig 2). A few cases also had true diverticula, some located in the region of the ureteric orifice.

*Shape and width of bladder neck.* The variations in the shape of the bladder neck are presented in Table 3. By constant distention is meant that at the time of each examination the neck was abnormally wide both in the resting state and throughout micturition, and usually was also funnel-shaped (Fig 2). The designation, intermittent distention, refers to the finding of an abnormally wide neck during some phase of urination at one or other of the examination periods. Analogous criteria apply regarding intermittent narrowing of the bladder neck (closed neck). Constant dilatation was never present when the lesion was of the



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Table 3

*Width of bladder neck at different levels of neurologic lesions*

| Level of neurologic lesion | Normal | Appearances of bladder neck |                         |                    |                        |
|----------------------------|--------|-----------------------------|-------------------------|--------------------|------------------------|
|                            |        | Constant distention         | Intermittent distention | Constant narrowing | Intermittent narrowing |
| Low thoracic               | 3      | 3                           | 0                       | 0                  | 0                      |
| High lumbar                | 1      | 5                           | 1                       | 2                  | 1                      |
| Low lumbar                 | 2      | 1                           | 0                       | 1                  | 0                      |
| High sacral                | 8      | 7                           | 4                       | 1                  | 1                      |
| Low sacral                 | 3      | 0                           | 0                       | 4                  | 0                      |
| Total                      | 17     | 16                          | 5                       | 8                  | 2                      |

Table 4

*Appearances of external sphincter of urethra at different levels of neurologic lesions present in boys and girls — + signifies mild obstruction, ++ denotes moderate narrowing resulting in slight reduction in width of urethra distal to the sphincter +++ indicates severely obstructive sphincter occasionally with total interruption of stream*

| Level of<br>neurologic<br>lesion | Appearances of external sphincter |              |                       |      |     | Total |
|----------------------------------|-----------------------------------|--------------|-----------------------|------|-----|-------|
|                                  | No con-<br>striction              | Intermittent | Constant constriction |      |     |       |
|                                  |                                   |              | +                     | ++   | +++ |       |
| Low thoracic                     | 1                                 | 2            | 2                     | 1    | 1   | 4     |
| High lumbar                      | 0                                 | 0            | 3                     | 4    | 2   | 9     |
| Low lumbar                       | 0                                 | 1            | 1                     | 2    | 0   | 3     |
| High sacral                      | 1                                 | 4            | 6                     | 7    | 3   | 16    |
| Low sacral                       | 0                                 | 1            | 1                     | 3    | 2   | 6     |
| Total                            | 2                                 | 8            | 13                    | 17   | 8   | 38    |
| Sex distribution<br>(boys girls) | 1 1                               | 5 3          | 7 6                   | 7 10 | 1 7 | 15 23 |

index. Marked sphincter obstruction was much commoner in girls than in boys. In one boy, only the diaphragmatic part of the urethral sphincter was narrowed while the entire posterior urethra presented evidence of slight fusiform dilatation (Fig. 2). The constriction at the level of the external sphincter was often combined with widening of the posterior urethra above the sphincter, as well as distention of the bladder neck (Figs. 2, 3 and 5). Only in one case was assessment of the external sphincter on the above mentioned basis made difficult by the



Fig. 4. Micturition urethrocytographs in myelomeningocele with cord lesion of high lumbar type. Girl 14 years old. Abnormal descent of elongated bladder through pelvic floor. Bladder with waist like narrowing and a pointed form. Normal bladder neck but urethra constricted by external sphincter.

low sacral type, and constant narrowing was never observed in connection with the highest level type. If the two uppermost lesion levels are considered together, 8 out of 16 cases had a constantly dilated, and more or less funnel shaped bladder neck, while the corresponding figures for the three lower levels were 8 out of 32 cases. It should also be mentioned that among the 16 cases with a constantly dilated neck, 11 were boys, whereas there was only one boy among the 8 cases with a constantly narrowed neck. Narrowing of the neck was related to a high infection index but there was no relationship to the age of the patients. All cases in which the neck was dilated during urination also had a dilated posterior urethra above the external sphincter.

*External sphincter of the urethra.* Constriction of the posterior urethra at the level of the external sphincter was a common finding in the micturition studies. A semi-quantitative grading of this feature is presented in Table 4. It was present constantly in 38 cases, intermittently in 8, and was wholly absent only in 2 cases. The severity of constriction of the external sphincter bore no relation to the level of the neurologic lesion, an obstructive external sphincter being present regardless whether other signs of intact reflex activity in the sacral cord were present or not. Similarly there was no relationship to age or infection

Table 5

*Vesico-ureteric reflux at different levels of neurologic lesions*

| Level of neurologic lesion | Vesico-ureteric reflux |        | Total |
|----------------------------|------------------------|--------|-------|
|                            | No reflux              | Reflux |       |
| Low thoracic               | 1                      | 5      | 6     |
| High lumbar                | 5                      | 5      | 10    |
| Low lumbar                 | 2                      | 2      | 4     |
| High sacral                | 10                     | 11     | 21    |
| Low sacral                 | 5                      | 2      | 7     |
| Total                      | 23                     | 25     | 48    |

unilateral reflux, the remaining 4 cases presented no signs of it. There was thus no unequivocal relation between the occurrence of hydro-ureter and reflux, nor was there any relationship to the presence of an obstructive external urethral sphincter.

### Discussion

An extensive, and in some measure contradictory, literature is available regarding the morphology and function of the urinary tract, and especially of the bladder in neurogenic disturbances. Different methods, such as excretion urography, urethrocystography, simple cystography, cystometry with pressure flow recordings, and electromyography, have been used either separately or in combination in these investigations. Divergent interpretations and conclusions may be partly explained by differences in the composition of the materials with respect to the etiology of the neurology, different lesion levels, the ages of the patients and so on. The findings and conclusions obtained from the use of excretion urography and micturition urethrocystography in cases of bladder dysfunction due to myelomeningocele also diverge among different authors.

The present investigation of the roentgen alterations in the urinary tract in children with myelomeningocele brought out certain leading features that to some extent agree well with the changes described by earlier workers. The bladder is usually elongated and the dome sometimes pointed, and the urethra may present varying degrees of narrowing at the level of the external sphincter. These abnormalities were recorded consistently in 40 and 38 cases, respectively, among a total of 48 cases. Thus none of the findings are invariably present, nor specific to neurogenic bladder dysfunction, but this combination of observations is uncommon in non neurogenic disturbance of the bladder, a peaked dome, however,

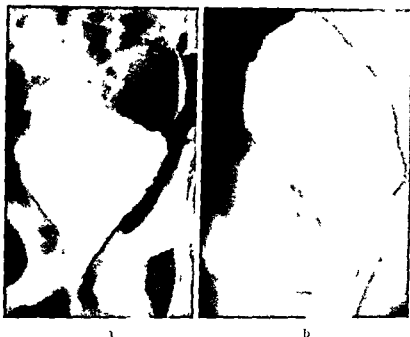


Fig. 5. Bladder and urethra in myelomeningocele with cord lesion of the high sacral type. Boy 11 years old. a) Excretion urography. Widely patent bladder neck. b) Micturition urethrocystography. Unusually wide, funnel-shaped bladder neck and only minor constriction of urethra.

strongly contracted bladder neck preventing a satisfactory flow through the urethra. The urethral narrowing persisted in 4 out of 7 cases, even when the pudendal nerve was anesthetized.

*Ureteric reflux.* Table 5 indicates the frequency of vesico-ureteric reflux during contrast filling of the bladder and subsequent urination. The series comprises all cases that had had uni- or bilateral reflux to the upper urinary tract on one or more occasions (Fig. 1). The reflux bore no relationship to the neurologic lesion levels, but was commoner in cases with frequent infections. No relationship with the appearances of the bladder neck, the severity of the obstruction in the external sphincter region nor the age or sex of the patients was established.

*Hydronephrosis and hydro-ureter.* Abnormal distention of the upper urinary tract was noted in 24 cases, 5 of these, however, had associated malformations of unknown significance from this viewpoint. It was unrelated to the level of the neurologic lesion, the age and sex of the patients and to the infection index. Among 19 cases with bilateral hydro-ureter 10 had bilateral reflux and 5 had

ROBERT's method of grouping was criticized by SMITH (1965) whose series consisted of 64 children with myelomeningocele, all of whom had undergone thorough urologic examination. An active detrusor, as well as a narrow bladder neck were common findings. The bladder neck region was described as funnel-shaped in practically all cases, both at urethrocystography and cystoscopy, and the interpretation put on this was that the pelvic floor was paralytic and the urethra consequently shortened. SMITH, following radiologic and manometric investigations, classified his cases into three groups, the first of which was characterized by constant incontinence and relatively low 'sphincteric resistance', in the second group, there was high 'sphincteric resistance', while the third, smaller group consisted of mixed cases. A suggestive link between this classification and the level of the lesion was considered likely. When the level was lumbar or lumbosacral, the external sphincter was usually relaxed, while with a sacral level it was generally 'resistant'. SMITH considered that this external sphincteric spasm was difficult to explain neurologically as the levator ani muscle for instance, which is innervated from the same segment, was parietic. However, the fact that blocking of the pudendal nerve and the administration of drugs reduced the resistance suggested that there was activity in the striated muscle.

SMART (1965) investigated 44 cases of spina bifida cystica in patients aged from 2 months to 19 years with a manometer technique and micturition urethrocystography. A spastic external urethral sphincter was observed in only 3 patients, aged 13, 14 and 19 years, respectively. They all had low spinal lesions "affecting only sacral nerves in a patchy and incomplete fashion".

HARLOWE et coll (1965) observed a series of myelomeningocele patients during the first two years of life with the aid of various urologic investigations, including roentgenography. The abnormal urethrocystograms indicated trabeculation, diverticula, vesico-ureteric reflux, a "neurogenic contraction ring", a hypertrophic bladder neck, and external sphincter spasm. The abnormal features did not change appreciably after the neonatal period. An analysis of the relation between the different findings and neurologic observations was apparently not made.

PELLMAN (1965), in a report on some 60 cases of neurogenic bladder in children, most of them with myelomeningocele, considered that those with reflux had only slight sensory or motor defects, or both, but at the same time had a higher incidence of severe trabeculation. The primary data connected with the roentgen examinations of the bladder were incompletely described, however.

A few recent investigations are of particular interest in this context. COOPER (1968) investigated bladder function in 112 cases of myelomeningocele by means of pressure flow measurements, simultaneous recording of the intra abdominal pressure, and electrical stimulation of the pelvic floor. Roentgenologic aspects were not mentioned, but a point of interest for the present discussion is that

is with few exceptions present only in association with a neurogenic bladder. These changes, as well as other less consistently occurring abnormalities such as bladder trabeculation, pseudo-diverticula, true diverticula, and reflux, vary from case to case and are probably influenced by factors other than the primary neurologic ones. The configuration of the bladder neck was of particular interest, the variations between different individuals in the series being especially large, with constant, usually funnel-shaped distention of the neck or complete closure, as the two extreme groups. A relation between the appearances of the bladder neck and the level of the neurologic lesion possibly existed, a wide neck occurred more often with high lesions while narrowing was found to occur more commonly with low levels. These observations differ from those of GIERTZ & LINDBLOM (1951), who described different types of micturition urethrocytograms in neurogenic bladder dysfunction, not particularly confined to myelomeningocele cases. Assuming that the bladder centre lies at the vertebral level of Th12—L1, they demonstrated that the neck tended to open incompletely in the presence of supra-nuclear lesions whereas it was wider than normal, and funnel shaped, when the lesions were located infranuclearly. The reason for the absence of agreement between the two series cannot be analyzed as no neurologic data were included in the paper by GIERTZ & LINDBLOM.

A survey published by ROBERTS (1962) is of more direct interest. This author classified the results obtained from cine cystoradiographic examinations, from the detrusor function observed and the appearances of the bladder neck in an unspecified hospital material consisting mainly of cases of myelomeningocele. He considered that a relation to the level of the lesion could be established. When the level was relatively high, the micturition centre became dissociated from higher control and a hyperactive detrusor resulted. This hyperactivity could, in his opinion, cause trabeculation and active dilatation of the neck. An open neck of this type was however also observed in cases with 'hypotonic detrusor', a hypothetic, passive distention of the bladder neck as a result of constriction at the external sphincter was suggested as an explanation. Infection of the bladder was considered capable of producing secondary constriction of the neck. As the presentation of the relevant data of the case material was incomplete, the hypotheses advanced are difficult to assess.

GRAT *et coll.* (1964) examined 50 cases of spina bifida and myelomeningocele by means of excretion urography and delayed cystography. Thirty-one cases had pathologic changes in the lower urinary tract in the form of trabeculation of the bladder wall, saccules, celluloses, diverticula, and dilatation of the vesical neck. As they did not carry out micturition investigations nor analyze the observations in relation to the neurologic changes and urologic findings, little idea of the clinical significance of the roentgenologic information can be formed.

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normal or partial detrusor action was demonstrated in two thirds of the cases, while an open bladder neck, assessed on the basis of pressure measurements in the bladder and rectum, and flow examinations during urination, was considered to be present in approximately one third of the cases. The bladder neck was of great significance to continence. A neurologic classification based on signs of upper or peripheral motor neuron lesions was in COOPER's opinion of little help as regards prognosis and treatment.

GROSSMAN *et coll.* (1968) stated that spina bifida with myelomeningocele in childhood characteristically produces a hypertonic bladder with a hypertrophied wall, trabeculae and diverticula and, at times, hourglass deformity of the bladder. The relations to the level of the neurologic lesion were not discussed.

WILLIAMS & JONES (1968) examined 38 infants during the first month of life by means of urography and micturition urethrocystography. Those with myelomeningocele had been treated surgically during the first day of life. Hydro-nephrosis was demonstrated in 7 infants, unilateral and bilateral reflux in 10, and trabeculation and diverticulum of the bladder in 19 infants. A dilated, funnel shaped bladder neck and posterior urethra was present in 9 cases, but no mention was made of the condition of the external urethral sphincter. No conclusions were drawn regarding a possible connection between the roentgen abnormalities in the urinary tract, and the level of the lesion.

An exhaustive analysis of the bladder function and its correlation with the neurologic data, was carried out by STARK (1968) in 40 cases of myelomeningocele followed from the neonatal period. A flaccid bladder with an inactive detrusor was noted in only one third of the cases. There was a high incidence of external sphincter spasm in those cases in which other forms of reflex action from the sacral cord were recorded, and a low incidence when no such activity could be established. The defective coordination between detrusor activity and external sphincter ('sphincter-detrusor dysynergia') was considered to be a significant factor in the neurogenic disturbance. Vesico-ureteric reflux was present at birth in slightly over 25 per cent of the cases.

EDWARDS *et coll.* (1968) made a roentgen analysis of neurogenic bladders in children, most of whom had myelomeningocele. As in the present series a high incidence of abnormally shaped bladders and of obstruction at the external sphincter was noted. The absence of vesical neck obstruction was emphasized. The external sphincter spasm in the boys was treated by sphincterotomy, in the girls urinary diversion procedures often had to be undertaken. No attempt was made to correlate the data with the neurologic observations or lesion level.

The conclusions reached in all these investigations can only in part be compared with the results in the present study, which were largely obtained by analyzing the findings at excretory urography and micturition urethrocystography. This

series revealed a high incidence of roentgenologic changes which admittedly were unspecific when taken separately, but when considered in combination were relatively characteristic. The typical features were elongation of the bladder, narrowing of the urethra in the external sphincter region, and an altered configuration of the bladder neck, ranging from abnormally wide to narrow, during urination. The incidence of vesico ureteric reflux and trabeculation of the bladder wall was high. The trabeculae occurred early in infancy and tended to become accentuated with age. As regards the changes in bladder shape and the presumed external sphincter spasm in the urethra there was no relation to the extent of the neurologic defects and the lesion level. The width of the bladder neck appeared to be dependent on the level of the neurologic lesion, high lesions, for instance, seemed to be a predisposing factor for a wide neck. No definite connection between the occurrence of a distended bladder neck and a low, parietic pelvic floor was demonstrated. The retention and infection of urine modified to some extent the roentgenographic appearances of both the upper and lower urinary tracts in the subsequent course. Further investigations in the neonatal period would probably provide more unequivocal information on the connection between the abnormal features in the roentgenograms of the urinary tract and the neurologic lesion.

## SUMMARY

An investigation has been made of the relationship between the appearances of the upper and lower urinary tracts examined by serial excretion urography and micturition urethrocystography and the neurologic changes and urologic data, in a series of 48 infants and children with myelomeningocele. The results of the analysis and the significance of the findings are described in detail.

## ZUSAMMENFASSUNG

An einer Serie von 48 Kindern, die an Myelomeningocele litten, wurde das Röntgenbild der unteren Harnwege mittels der Ausscheidungsurographie und cystographischen Bildern während des Urinierens studiert und mit den neurologischen und urologischen Befunden verglichen. Die Resultate und charakteristischen Befunde werden detailliert beschrieben.

## RÉSUMÉ

Les auteurs ont étudié la relation entre l'aspect des voies urinaires supérieures et inférieures examinées par urographie excrétrice en série et par urethrocytographie mictionnelle d'une part et les troubles neurologiques et urologiques d'autre part sur une série de 48 nourrissons et enfants atteints de myelomeningocele. Les résultats de cette analyse et l'intérêt de ces constatations sont décrits en détail.

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## UROGRAPHY IN RENAL FAILURE

by

P STAGE, E BRIK, K FOLKE and A. KARLE

Urography was generally a poor diagnostic procedure in renal insufficiency before the introduction of the triiodized contrast agents and commonly entailed the risk of producing further impairment of renal function (OLSSON 1954). Its diagnostic value has been increased in recent years by the use of relatively large doses of the media (BARTLEY et coll 1968, 1969, FULTON et coll 1969, FRIEDENBERG & CARLIN 1964, ROSS et coll 1964, SCHWARTZ et coll 1963). This improved technique has not been accompanied by renal damage.

These findings, however, have apparently not been generally accepted or appreciated by all radiologists and clinicians. The diagnostic value of high dose urography is limited by the side effects of the examination on the renal function.

Firstly by the side effects of the examination on the renal function and secondly by recording the side effects of the examination on the renal function.

*Material and Methods* The material comprised 225 patients with renal failure in whom a total of 258 urographies were performed. The dosage of sodium methylglucamine diatrizoate (Urografin 76 %) was regulated according to body weight and serum creatinine level (Table 1).

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Table 1

*Relationship between serum creatinine level in mg/100 ml, body weight in kg and dose in ml of Urografin 76<sup>®</sup>*

| Creatinine mg/100 ml | 40—55 kg | 55—70 kg | > 70 kg |
|----------------------|----------|----------|---------|
| 1.6—2.0              | 80       | 100      | 120     |
| 2.1—2.5              | 100      | 120      | 150     |
| 2.6—3.0              | 120      | 150      | 150     |
| > 3.0                | 150      | 150      | 150     |

Table 2

*Distribution according to age and sex of patients in 258 urographies*

| Years   | 10—19 | 20—29 | 30—39 | 40—49 | 50—59 | 60—69 | 70—79 | 80—89 |
|---------|-------|-------|-------|-------|-------|-------|-------|-------|
| Males   | 2     | 14    | 11    | 18    | 44    | 33    | 40    | 2     |
| Females | 2     | 3     | 9     | 11    | 35    | 28    | 5     | 1     |

Table 3

*Distribution according to creatinine level before examination and technique of contrast administration in 258 urographies*

| Creatinine mg/100 ml | Injection* | Infusion** | Total |
|----------------------|------------|------------|-------|
| 1.6—2.0              | 53         | 39         | 92    |
| 2.1—2.5              | 34         | 23         | 57    |
| 2.6—3.0              | 20         | 21         | 41    |
| 3.1—4.0              | 19         | 8          | 27    |
| 4.1—5.0              | 10         | 6          | 16    |
| 5.1—6.0              | 7          | 4          | 11    |
| 6.1—7.0              | 3          | 0          | 3     |
| 7.1—8.0              | 3          | 1          | 4     |
| 8.1—9.0              | 0          | 0          | 0     |
| 9.1—10.0             | 3          | 1          | 4     |
| 10.1—11.1            | 1          | 2          | 3     |
| Total                | 153        | 105        | 258   |

\* Intravenous injection of undiluted contrast medium administered over 2—5 minutes

\*\* For intravenous infusion the dose of contrast medium was diluted with 150 ml isotonic dextrose solution and given as drip infusion over 8—12 minutes

The investigation was carried out during the period 1966 to 1969 and included all adult patients with creatinine concentration of 1.6 mg/100 ml or higher. Patients in whom a moderate increase in serum creatinine level could be explained as resulting solely from dehydration were excluded (Range of normal serum creatinine in this hospital: males 0.7—1.5 mg/100 ml, females 0.5—1.3 mg/100 ml).

Prior to the examination, the patients were purged and kept without food overnight. The contrast medium was given undiluted by rapid manual injection (153 patients) during one period, during a later period, 150 ml dextrose 5% were added to the contrast medium and administered as a drip infusion over 8 to 12 minutes (105 patients). No ureteric compression was applied and films were obtained 5, 10, 20 and 30 minutes and 1, 3, 6 and 24 hours after the injection. Tomography was not performed.

The films were evaluated by the four authors conjointly, and the case records were subsequently reviewed. The serum creatinine concentration was measured before and after the examination for assessment of possible further functional renal impairment following the examination.

The age and sex distribution of the series are presented in Table 2 and the examinations are grouped according to serum creatinine levels and injection or infusion techniques in Table 3. The distribution of the 225 patients according to diagnosis at discharge was as follows:

|  |     |
|--|-----|
| Chronic pyelonephritis   | 126 |
| (with papillary necrosis in 30, concrements in 27, marked prostatic hypertrophy in 16, congenital megaureter in 4, neurogenic bladder in 1, and retroperitoneal fibrosis in 1) |     |
| Chronic glomerulonephritis   | 17  |
| Acute glomerulonephritis   | 3   |
| Collagenosis   | 5   |
| Hypertensive nephropathy   | 14  |
| Ischaemic nephropathy  | 6   |
| Polycystic kidney  | 6   |
| Hyperparathyroidism  | 8   |
| Urolithiasis   | 5   |
| Tuberculosis   | 2   |
| Nephropathy of undetermined nature   | 10  |
| Bladder tumour   | 11  |
| Carcinoma of the prostate  | 8   |
| Renal carcinoma  | 1   |
| Myelomatosis, paraproteinaemia   | 2   |
| Malignant lymphogranulomatosis   | 1   |

Table 4

*Relative frequency (%) of diagnostic demonstration of details of the urinary tract in relation to creatinine levels prior to urography*

| Creatinine<br>mg/100 ml         | 1.6—2.0 | 2.1—2.5 | 2.6—3.0 | 3.1—4.0 | 4.1—6.0 | 6.1—8.0 | >8.0 |
|---------------------------------|---------|---------|---------|---------|---------|---------|------|
| Number of<br>examinations       | 92      | 57      | 41      | 27      | 27      | 7       | 7    |
| Renal<br>parenchyma             | 94      | 90      | 95      | 90      | 83      | 57      | 64   |
| Calyx system                    | 91      | 90      | 78      | 75      | 47      | 21      | 14   |
| Renal pelvis                    | 98      | 95      | 97      | 94      | 85      | 50      | 50   |
| Ureter                          | 97      | 91      | 95      | 85      | 90      | 43      | 43   |
| Bladder                         | 99      | 97      | 98      | 91      | 100     | 72      | 100  |
| All structures<br>on both sides | 78      | 70      | 68      | 18      | 33      | 0       | 0    |

## Results

*Evaluation of the urographic examination* The demonstration of a number of specified details was evaluated in all 258 urographics and each classified as diagnostically sufficient or diagnostically insufficient. The term 'diagnostically sufficient' indicates (1) accumulation of contrast medium within the parenchyma enabling total delineation of the kidney, (2) a concentration of contrast medium in the urinary efferent system enabling the diagnosis of displacement and clubbing of calyces, outlining of the renal pelvis, ureter and bladder, respectively, and the recognition of stenoses and moderate filling defects. Table 4 indicates the correlation between different levels of serum creatinine and frequency of adequate demonstration of the urographic details mentioned. The frequency of diagnostic sufficiency is expressed as a percentage to facilitate a general survey.

*Obstruction of urinary system* Partial obstruction was diagnosed in a total of 57 patients and complete unilateral occlusion in 5 patients. In no patient did the subsequent course indicate false positive or negative diagnoses of obstruction.

The 190 examinations performed in patients with serum creatinine values below 3.1 mg/100 ml were all sufficient for the recognition of obstruction in the urinary system. In 4 out of 54 examinations, performed in patients with serum creatinine values ranging from 3.1 to 6.0 mg/100 ml, the demonstration was so poor that possible unilateral urinary obstruction could not be eliminated. Eight out of 14 examinations in patients with serum creatinine values higher than 6.0 mg/100 ml were inadequate, in 5 of them on both sides and in 3 on one side. The subsequent course failed to suggest obstruction in any of the 12 unsuccessful examinations.

Table 5

*Number of examinations distributed according to creatinine ranges before urography and the maximum increase in serum creatinine level on the first or second day after examination*

| Creatinine value<br>before urography<br>mg/100 ml | Number of<br>examinations | Increase in creatinine mg/100 ml |         |         |         |      |
|---|---------------------------|----------------------------------|---------|---------|---------|------|
|   |                           | —0.6/0.3                         | 0.4/0.6 | 0.7/1.1 | 1.2/1.9 | >1.9 |
| 1.6—3.0   | 182                       | 148                              | 16      | 11      | 5       | 2    |
| 3.1—6.0   | 54                        | 29                               | 6       | 9       | 8       | 2    |
| >6.0  | 14                        | 5                                | 3       | 2       | 3       | 1    |

Table 6

*Number of examinations distributed according to creatinine ranges before urography and increases in creatinine level approximately one week after examination*

| Creatinine value<br>before urography<br>mg/100 ml | Number of<br>examinations | Increase in creatinine mg/100 ml |         |         |         |      |
|---|---------------------------|----------------------------------|---------|---------|---------|------|
|   |                           | —2.0/0.3                         | 0.4/0.6 | 0.7/1.1 | 1.2/1.9 | >1.9 |
| 1.6—3.0   | 154                       | 145                              | 5       | 0       | 0       | 4    |
| 3.1—6.0   | 44                        | 35                               | 2       | 3       | 1       | 3    |
| >6.0  | 11                        | 5                                | 1       | 1       | 2       | 2    |

*Filling of the gallbladder* The correlation between the frequency of any contrast medium in the gallbladder or intestine and the serum creatinine level is indicated below

|                        |         |         |         |         |      |
|------------------------|---------|---------|---------|---------|------|
| Creatinine mg/100 ml   | 1.6—2.0 | 2.1—2.5 | 2.6—4.0 | 4.1—6.0 | >6.0 |
| Filling of gallbladder | 3 %     | 15 %    | 20 %    | 33 %    | 77 % |

Filling of the gallbladder usually did not occur until 24 hours after the injection

*Immediate side effects* No severe reactions were observed. Excluding slight nausea, sensation of heat or abnormal taste, which were not recorded, transient side effects were listed during 29 examinations (11.3 %): nausea in 4, nausea and vomiting in 12, dizziness in 5, urticaria in 3, severe sneezing in 1, low back pain in 1, angina pectoris in 1 and rise in temperature in 2 examinations. The frequency was not dependent on the technique of administration, i.e. injection in 12 and infusion in 10 % of the examinations.

*Change in the serum creatinine after urography* The serum creatinine levels were measured not more than five days before the examination and on the first



Table 4

*Relative frequency (%) of diagnostic demonstration of details of the urinary tract in relation to creatinine levels prior to urography*

| Creatinine<br>mg/100 ml         | 1.6—2.0 | 2.1—2.5 | 2.6—3.0 | 3.1—4.0 | 4.1—6.0 | 6.1—8.0 | >8.0 |
|---------------------------------|---------|---------|---------|---------|---------|---------|------|
| Number of<br>examinations       | 92      | 57      | 41      | 27      | 27      | 7       | 7    |
| Renal                           |         |         |         |         |         |         |      |
| parenchyma                      | 94      | 90      | 95      | 90      | 83      | 57      | 64   |
| Calyx system                    | 91      | 90      | 78      | 75      | 47      | 21      | 14   |
| Renal pelvis                    | 98      | 95      | 97      | 94      | 85      | 50      | 50   |
| Ureter                          | 97      | 91      | 95      | 85      | 90      | 43      | 43   |
| Bladder                         | 99      | 97      | 98      | 91      | 100     | 72      | 100  |
| All structures<br>on both sides | 78      | 70      | 68      | 48      | 33      | 0       | 0    |

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although it was unlikely. The second of the two patients was suffering from ischaemic nephropathy that developed 14 days prior to urography but apparently in rapid regression as the serum creatinine value had decreased gradually from 9.1 to 3.0 mg/100 ml on the day of examination. Following the urographic examination the serum creatinine level gradually increased over 7 days to 4.6 mg/100 ml. The initial value of 3.0 mg/100 ml was not obtained until 21 days, it later reached normal levels.

The frequency of a transient increase in a serum creatinine level higher than 0.6 mg/100 ml did not seem to depend on the technique of injection: infusion in 19 and injection in 16 % of patients.

Finally, a transient increase in serum creatinine level lasting from 2 to 7 days was not uncommon, although this never resulted in a permanent impairment of renal function, the transient increase lasted more than one week in only one patient.

In one out of two patients, subsequently considered to have paraproteinaemia, the examination was followed by transitory oliguria which may occur in myelomatosis after dehydration.

### Discussion

The triiodized contrast agents are excreted by glomerular filtration and consequently the dosage schedule was fixed according to the serum creatinine level and body weight. However, the maximum dose of 150 ml Urografin 76 % was administered to all patients with serum creatinine values higher than 3.0 mg/100 ml. A dosage higher than the one previously employed was administered with the object of improving the contrast.

It is difficult to compare the diagnostic content of the examination in different publications. SCHWARTZ *et coll* (1963), however, applying a comparable technique, were able to diagnose possible obstructions in only 5 out of 20 patients with serum creatinine levels higher than 5.0 mg/100 ml. They administered a lower dose of contrast medium, 60 ml Hypaque 50 %. It may be concluded that the definition is improved by increasing the dose. This is in agreement with previous authors, DOYLE *et coll* (1967) and SHERWOOD *et coll* (1968).

The present diagnostic results in patients with serum creatinine levels lower than 6.0 mg/100 ml do not seem to have been surpassed by other workers. FULTON *et coll* (1969) obtained results better than the present ones in patients with more marked renal failure, with a dose of contrast medium about 20 % lower (100 ml Hypaque 90 %). Their technique, however, included tomography, and hence was not.

It has been demonstrat

and second days after the urographic examination in 250 patients and approximately one week (4 to 14 days) following urography in 219 out of the 258 patients, the remainder having been discharged before these determinations could be performed.

Statistically significant mean increases of serum creatinine amounting to 0.11 and 0.14 mg/100 ml on the first and second days, respectively, ( $p < 0.01$ ) were recorded in relation to the serum creatinine levels prior to urography. A statistically insignificant decrease of the mean of the serum creatinine level amounting to 0.04 mg/100 ml was noted at the later examination. The distribution of examinations according to their maximum change in serum creatinine level on the first or second day, as compared to the level prior to urography, appears in Table 5. The distribution of examinations according to their change in serum creatinine level at the later examination, as compared to the level prior to urography is presented in Table 6. Hence in 43 patients (17%) the serum creatinine value was increased by more than 0.6 mg/100 ml on the first or second day but was never decreased by more than 0.6 mg/100 ml. At the later examination the value remained increased by more than 0.6 mg/100 ml in 16 patients (7%). In other words, the urography was often followed by a transient increase in the serum creatinine level of less than one week's duration but in 16 patients an increase of over 0.6 mg/100 ml was still observed at the later examination. In all these 16 patients several serum creatinine values obtained prior to urography were available, and the subsequent course was checked by repeat measurements of the values until a reasonable explanation was established.

Fourteen of the 16 patients had rapidly progressive uraemia prior to urography. A temporary additional increase in the serum creatinine, lasting from 2 to 7 days, was observed in all these patients. After this period the serum creatinine level returned to the same progressive curve as that before the examination in 9 of the patients. In the remaining 5 patients the serum creatinine level later decreased to values below the initial level following surgical correction of the urinary obstruction and the administration of antibiotics (for acute pyelonephritis) or of prednisone (for periarteritis nodosa). No permanent impairment of renal function appeared to have been caused by the urography in these patients.

The last two of the 16 patients had non-progressive uraemia before urography. The examination was followed by an initial increase in the serum creatinine from 3.0 to 3.5 mg/100 ml in the first patient who was suffering from chronic pyelonephritis. Two days after urography he developed profuse gastric haemorrhage with intractable shock and died ten days later in anuria. Whether the haemorrhage was provoked by the examination cannot be determined.

at serum creatinine levels up to 60 mg/100 ml although valuable data were usually recorded at higher levels. The examination was often followed by a transient increase in the serum creatinine level but never resulted in permanent reduction in renal function.

## ZUSAMMENFASSUNG

Insgesamt wurden 208 Urographien mit ziemlich grossen Kontrastmittelmengen an 225 Patienten mit Azotämie vorgenommen. Befriedigende diagnostische Resultate konnten ohne Tomographie bei Serumkreatininspiegeln bis zu 60 mg/100 ml erhalten werden, obwohl wertvolle Resultate auch bei höheren Spiegeln erzielt wurden. Eine vorübergehende Erhöhung des Kreatininspiegels zeigte sich öfters nach der Untersuchung; andauernde Nierenschädigungen wurden jedoch nicht beobachtet.

## RÉSUMÉ

Les auteurs ont fait un total de 208 urographies chez 225 malades azotémiques en utilisant des doses de moyens de contraste relativement importantes. Ils ont obtenu des résultats satisfaisants pour le diagnostic sans tomographie jusqu'à des taux de créatinine sérique atteignant 6 mg pour 100 ml; cependant des résultats utiles ont été obtenus habituellement même avec des taux plus élevés. L'examen a été souvent suivi par une élévation transitoire du taux de créatinine sérique mais n'a jamais entraîné une réduction permanente de la fonction rénale.

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to protein are excreted through the liver and that in renal failure, this excretion may increase so that the gallbladder becomes filled (CHAMBERLAIN & SHERWOOD 1966). It was possible to demonstrate in the present series that filling of the gallbladder increases with the degree of renal failure, the liver thus acting as a sort of safety valve.

The immediate side effects attributed to the contrast medium were all of a temporary nature and did not require treatment and consequently do not contra-indicate the employment of large doses of contrast. The results fail to agree with those obtained by DOYLE *et coll.* and SHERWOOD *et coll.*, who were unable to make examinations with doses of the same order of magnitude on account of immediate marked side effects, including generalized tremor. The present relatively high incidence of mild side effects may be due to the large dose of contrast medium administered and the poor general condition of most of the patients.

Previous reports have been unable to indicate indisputable cases of permanent impairment of renal function, following large-dose urography in renal insufficiency (BARTLEY *et coll.* 1969, FULTON *et coll.* 1969, ROSS *et coll.* 1964, SCHWARTZ *et coll.* 1963). Transient impairment is described only by SCHWARTZ *et coll.* A temporary increase in the serum creatinine level of up to one week's duration occurred in 4 out of 90 patients following the administration of 60 ml Hypaque 50 %.

The findings are in the main identical to those of SCHWARTZ *et coll.* However, the incidence of transient increase in serum creatinine in the present material was higher than theirs, which seems to correspond with the higher dose of contrast medium employed. In neither of the materials did the use of large-dose urography result in permanent reduction of renal function. This transitory 'nephrotoxic' effect could not be explained. However, according to GUR *et coll.* (1966) the administration of triiodized contrast agents to healthy subjects seems to cause a temporary reduction in renal plasma flow and glomerular filtration. This mechanism may probably be the cause of the transitory reduction of renal function in azotemic patients.

It is noteworthy that the technique of injection did not influence the frequency of adequate demonstration, the incidence of side effects or a temporary increase in serum creatinine levels. Any final conclusion regarding the superiority of any one type of administration appears however impossible on account of the inhomogeneity of the series.

## SUMMARY

A total of 258 urographies were performed in 225 azotemic patients with relatively large doses of contrast medium. Adequate diagnostic results were obtained without tomography.

*Material and Methods* The present series consisted of 115 patients, 55 boys and 60 girls, being part of a consecutive series of chest examinations. Excluded were those patients in whom clinical or radiologic evidence of disease might account for the presence of pleural fluid. The age range was from 7 days to 18 years with a mean of 6.4 years and a median age of 6 years.

All patients below the age of 6 years were examined supine and older children in the erect position. The routine examination included two a p or p a films of the lungs, one obtained with penetrating rays to permit evaluation of the mediastinum and retrocardiac region, and one true lateral view. In this series the standard projections were supplemented by left and right lateral decubitus films with a horizontal beam, the central ray being directed at the lowermost part of the chest.

The recognition of a mantle shaped pleural thickening along the dependent lateral chest wall, not demonstrable in the standard projections or changing appearance with the projection used, was interpreted as produced by fluid in the pleura.

Subjects with unexplained free pleural fluid were re-examined and their history re-analysed 5 years later.

### Results

Unilateral pleural fluid was demonstrated at the initial examination in four patients: two girls and two boys, aged 3, 4, 5 and 7 years, respectively. In two of these the fluid was present on the right side and in two on the left side. In a boy of 7 years there was fluid in both pleurae. The maximum thickness of the fluid layers was assessed as 1.5 to 2 mm. In none of the above mentioned patients was there any clinical or radiologic evidence of disease to explain the unexpected presence of pleural fluid.

No pleural fluid was demonstrated in four of the patients at the re-examination performed 5 years later. The amount of fluid was however essentially unchanged in one patient. The radiologic examination revealed no pulmonary, hilar or mediastinal lesions.

### Discussion and Conclusions

The normal pleura contains only a few milliliters of fluid, probably sufficient to serve lubricating purposes but generally considered too small for radiologic recognition. MULLER & LOFSTEDT (1945) and HESSEN (1951) reported however that the fluid may occur in quantities large enough to be demonstrated radiologically. The technique recommended — films exposed with a horizontal beam

## PLEURAL FLUID IN HEALTHY CHILDREN

by

OLE EKLOF and ANDERS TORNGREN

The pleura in healthy children, because of its tenuity, has been regarded as radiologically invisible. Consistent with this conception any pleural thickening, and particularly if associated with effusion, has been considered to indicate an underlying disease process (CARRFY 1967, HICH 1967). Tuberculous infection earlier played a significant role among the manifold causes of free pleural fluid. LINCOLN & SWEET in 1963 and KENDIG in 1967 were still suggesting that the finding of a pleural effusion in a child with a positive tuberculin test should be interpreted as tuberculous until proved otherwise.

HESSLEN, however, as early as 1951, demonstrated the occasional occurrence of free pleural fluid unassociated with symptoms or signs of cardiac or pulmonary disease in twelve out of three hundred patients who all with the exception of some ten were adolescents or adults. It would appear that no report has as yet been published of radiologically demonstrated pleural fluid in healthy children, at least not below the age of 10 years.

The aim of this investigation was to estimate the occurrence and evolution of small amounts of pleural fluid unassociated with disease discovered at roentgen examination of the chest of infants and children.

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Submitted for publication 26 March 1970

positive tuberculin test does not clinch the diagnosis, not so particularly in countries in which all newborn infants are vaccinated with BCG. In the absence of evidence of disease, small quantities of pleural fluid may be physiologic.

### Acknowledgement

Financial support from the Swedish National Association against Heart and Chest Diseases is gratefully acknowledged.

### SUMMARY

One hundred and fifteen young children underwent routine radiologic chest examinations supplemented by films in both lateral decubitus positions with a horizontal beam. Small amounts of pleural fluid were demonstrated in five otherwise healthy subjects. The significance of this finding is discussed.

### ZUSAMMENFASSUNG

Einhundertfünfzehn junge Kinder wurden einer routinemässigen radiologischen Thoraxuntersuchung unterzogen wobei dieselbe mit Aufnahmen in beiden lateralen Decubituslagen mit horizontaler Strahlenrichtung ergänzt wurde. In fünf ansonst gesunden Individuen wurden kleine Mengen von pleuralen Ergüssen festgestellt. Die Bedeutung dieses Befundes wird besprochen.

### RÉSUMÉ

Cent quinze  
completes par c  
Les auteurs ont

été en par ailleurs en de la santé. Les auteurs discutent l'importance de cette constatation.

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and the patient in an inclined lateral decubitus position — enabled MULLER & LOFSTEDT to recognize fluid in quantities as small as between 3 and 5 milliliters, as proved by thoracocentesis

The amount of pleural fluid that may be present in physiologic conditions is subject to individual variations. The relative frequency of radiologically demonstrable quantities, about 4 per cent, seems to be the same in all age groups, as evaluated from the present series and the one of HESSEN. The factors apt to influence the evolution of this fluid are as yet inadequately known. Differences in the examination technique and a different phase of respiration at the moment of exposure may to some degree explain incongruous findings at consecutive examinations of one and the same patient. The statement of e.g. VOCI (1962) that the smallest radiologically discernible quantity of pleural fluid amounts to 100 milliliters is obviously incorrect. A faulty examination technique would account for this error. Remarkably enough, the lateral decubitus position for the demonstration of pleural fluid is not generally utilized in radiologic practice. Furthermore, recent textbook writers pay little or no attention to this projection (LINCOLN & SEWELL 1963, CAFIFI 1967, KENDIG 1967).

It should be stressed in this connection that the interlobar pleura, particularly that of the right lung, may ordinarily be visible in chest films of infants and children but this finding is not necessarily of pathologic significance.

The patients included in our series attended hospital for a physiologic heart murmur, a known congenital heart lesion, asthma, upper respiratory tract infection, or for a health check. The diagnosis established in the five patients with fluid in the pleura was of a physiologic heart murmur, in one combined with respiratory arrhythmia. Neither clinical nor radiologic examinations revealed evidence to account for the finding of fluid in the pleura, it was therefore interpreted as a physiologic variation of the pleural content. Re examination 5 years later in one patient revealed apparently unchanged conditions. This is consistent with the experience of HESSEN, i.e. that physiologic pleural effusions may be demonstrated on repeat chest examinations.

The rule stressed by several authors (LOWELL 1959, LINCOLN & SEWELL 1963, KENDIG 1967), invariably to consider pleural effusions as a manifestation of disease, seems to be based on the assumption that only large quantities of fluid are radiologically demonstrable. As indicated by MULLER & LOFSTEDT in adults, by HESSEN in adolescents and adults, and by the present authors in infants and children, films exposed in the lateral decubitus position with a horizontal beam enable the radiologist to establish the occasional occurrence of extremely small amounts of pleural fluid. The conclusion made by HESSEN that a diagnosis of tuberculous pleurisy, in otherwise healthy patients, cannot be based solely on the presence of pleural fluid should equally apply to infants and children. Even a

**GOLDEN'S DIAGNOSTIC RADIOLOGY Section 5 Digestive tract** By R. Golden, C. V. Cimmino, L. C. Collins, J. R. Dreyfuss and M. L. Janower. Edited by L. L. Robbins. 942 pages with 632 figures. Williams & Wilkins Co., Baltimore 1969. Price US \$ 41.50.

This section, revised after nine years, comprises about 900 pages and 632 illustrations well selected and of excellent quality. It is always difficult to decide how much should be included in a textbook: too many details should be avoided and yet the chapters must be complete and up to date. Much important information makes this book extremely valuable. The typical cases that are presented and compared from a pathologic standpoint indicate that diagnostic radiology is in reality pathology *in vivo*.

Lesions of the oesophagus are described and the controversial region of the cardia is considered. It is however somewhat surprising to find the incidence of hiatus hernia given as 5 to 15 per cent. The examination technique of the stomach and duodenum seems to be a little old-fashioned: the double-contrast method is seldom used and a comparison of the value of gastroscopy to that of radiology is conspicuous by its absence. Hypotonic duodenography is mentioned but no illustrative cases are included. The value of angiography finds no place in the text.

The chapter on the small intestine is impressive and must represent a valuable source of information to those working in this field. The same applies to the large bowel which has mostly been examined by conventional barium enemas. However, the double-contrast method has here been well presented and its superiority, particularly in polyps, is beautifully proved. The book can be recommended both for senior radiologists and as a reference textbook.

J. Frimann Dahl

**RADIOLOGIC EXAMINATION OF THE COLON** By J. R. Dreyfuss and M. L. Janower. 124 pages with 130 figures. Williams & Wilkins Co., Baltimore 1969. Price US \$ 9.75.

The book consists of the final part of Section 5. The digestive tract from Golden's Diagnostic radiology. It is unusual in Europe to encounter parts of a text book printed and bound for sale in place of a limited number of reprints for the author or authors. Without doubt the handling of a small book is easier than the large volume from which it is taken.

An initial chapter deals with the anatomy and physiology. The preparation of the colon is carefully discussed. Castor oil and cleansing water enemas are recommended as superior to the various substitutes. The authors also discuss the use of the balloon retention catheter, as well as the problem of tannic acid enemas.

Diverticular disease of colon is specially dealt with and discussed from the point of view of new concepts. Increased colonic motor activity is considered to be the etiologic agent in the production of diverticulosis that formerly was thought to be secondary to acute or chronic inflammation. Consequently the term *the irritable colon syndrome* has been lifted from the depths of degradation and may be regarded as a missing link in the chain responsible for the unusually high pressures in colons that subsequently develop diverticulosis and diverticulitis.

In the section on inflammatory diseases the authors discuss

## Book reviews

**OTORHINOLARYNGOLOGIC RADIOLOGY. A RADIOLOGIC ATLAS OF EAR, NOSE AND THROAT DISEASES**  
By R. Mittermaier. 403 pages with 694 figures. Georg Thieme Verlag, Stuttgart 1970  
Price: DM 140

There are few books on otorhinolaryngologic radiology. A translation in the English language of the third German edition of this work is consequently of considerable interest. The sub-title, 'A radiologic atlas of ear, nose and throat diseases' however, constitutes a warning signal. Most radiologic atlases usually contain roentgenograms of various conditions and tend to disappoint. This work is no exception.

The book consists of 430 cases illustrated with 694 roentgenograms and accompanied by a short clinical history as well as a description of the roentgen findings. It is claimed in the preface that the illustrations may be used by the clinician as well as by the radiologist as sources of comparison. Nothing could be further from the truth. A similar 'museum' can easily be collected from most roentgen departments and little is gained by comparing a film from one examination with one from another. Proper diagnostic ability can be gained only by a thorough knowledge of the anatomic, pathologic and clinical aspects of the various diseases.

The book is old-fashioned in the roentgenologic technique used, i.e. modern diagnostic procedures in examining the middle and inner ear are entirely absent. Tomography is mentioned and also illustrated in a few cases but nothing of interest is said regarding the recent progress with hypocycloid tomography in diseases of the middle and inner ear.

Although most illustrations are of good quality, many are nevertheless not good enough to permit of the conclusions drawn by the author, not to mention those cases in which the roentgen appearances described and the projection employed do not tally. Two examples will suffice. Changes in the frontal sinuses are discussed although the illustrations are usually produced by a projection unsatisfactory for the examination of these sinuses. Schuller's or Stenvers' views are used in acoustic neuromas although it is well known that they are the least suitable ones.

The roentgen examination of the paranasal sinuses take the largest part of the book and other organs of interest are only scantily treated. The salivary glands, the larynx and vocal cords and the hypopharynx, for example are covered only by a few illustrations. Fractures of the facial bones are presented in an incomplete way, i.e. the nasal bones are examined only with a lateral view. The significance of tomography in detecting blow-out fractures of the orbita is not mentioned.

A book composed of a variety of pathologic cases illustrated with roentgen films and corresponding clinical notes to be of any help to radiologists should be based upon a modern technique and cover all aspects of the topic. This work does not fulfil those requirements.

*Bengt Lihquist*

## ANGIOGRAPHY IN RUPTURE OF THE LIVER

by

T AAKHUS and J ENGE

The rising frequency of abdominal injuries is making the diagnosis of visceral ruptures increasingly important. Several authors have stressed the value of angiography in the diagnosis of rupture of the kidneys (OLSSON & LUNDERQUIST 1963, ELKIN et coll 1966, WENEAU et coll 1966, SCHREIBER et coll 1968, and others) and the spleen (NORELL 1957, ÖDMAN 1958, POLLARD & NEBESAR 1964, BALM et coll 1965, AAKHUS & ENGE 1967, and others). The high mortality in cases of hepatic rupture and the difficult diagnosis, often even at operation, emphasize the need for accurate investigation in this condition. FRIMANN-DAHL (1960) and McCORT (1966) described in detail the indirect findings obtained by conventional roentgenography; it would appear however that more direct information may be obtained by angiography.

BOITSEN et coll (1966) reported 5 cases of hepatic rupture with angiographic findings of (1) displacement of arteries, (2) accumulation of contrast medium in the hepatic substance, portal vein radicles or biliary ducts, and (3) displacement of adjacent viscera. Similar findings were reported by REDMAN et coll (1969), and specific descriptions of the angiographic findings in traumatic haemobilia were given by HERMANN & HOERR (1967) and ENGE et coll (1968). This condition may be revealed by direct demonstration of leakage of contrast medium from the arterial to the biliary tree.

From the Roentgen Department of Ullevål Sykehus (Director Prof J Frimann Dahl) and Rikshospitalet (Director Prof T Dale), Oslo, Norway. Submitted for publication 8 July 1970.

tion although they in no way neglect the known signs of possible malignancy and the importance of repeated observations. Carcinoma and certain rare tumours are discussed followed by a chapter on vascular diseases. The importance of the inferior mesenteric artery as a major collateral channel to the entire lower part of the body in some subjects is stressed. They also emphasize the impossibility of distinguishing between ulcerative or granulomatous colitis and a vascular accident if a long segment of colon is involved.

The appendix has its own chapter. The authors discuss useless and useful signs in appendicitis and consider that the diagnosis can be made with a barium enema when changes are demonstrated in the cecum in the immediate region of the appendiceal stoma.

Obstruction and injuries are treated shortly and the book finishes with miscellaneous and rare conditions.

The book is easy to read and contains much information. The high density of the barium enema in many of the illustrations tends to obscure detail, however, these are so selected that they are nevertheless instructive. The Scandinavian literature on the subject appears to be referred to in the bibliography with prejudice.

Nils P. G. Edling

VENOGRAPHY OF THE INFERIOR VENA CAVA AND ITS BRANCHES. By E. J. Ferris, F. A. Hipona, P. C. Kahn, E. Philipps and J. R. Shapiro. 229 pages with 138 figures. William & Wilkins Co., Baltimore, 1969. Price US \$ 16.

This monography by five members of the faculty of the great Boston medical schools may act as a good counterbalance and supplement to the overwhelming literature on arteriography of the abdominal organs. The first chapter on embryology, normal anatomy and anomalies (by Philipps) is illustrated with many good composite diagrams in colour explaining the natural history of developmental errors and anatomic variations so often met with on the venous side of the vascular system. The second chapter on techniques and pitfalls in interpretation (by Hipona) is introduced with a short history of cavography and followed by a description and evaluation of the different methods used by the authors. Included are capnoscavography (with 60 to 100 ml pure carbon dioxide), double contrast cavography, biocclusive cavography, angioscanning and ultrasonography with a velocity detector. Misleading artefacts encountered are exemplified and correlated with anatomic structures as well as with the streaming of blood from tributaries under different circumstances.

Various types of intrinsic obstruction (by Ferris) and extrinsic occlusion (by Shapiro) are described in two abundantly illustrated chapters. Selective phlebography of the branches is thoroughly and well documented by Kahn in a large final chapter, which will be most consulted when this technique that adds considerable diagnostic potential in troublesome cases, is employed. Carcinoma of the pancreas may be verified by selective left renal phlebography. Each chapter is followed with up to-date references and many European, including Scandinavian, authors are cited.

A confusing editorial mistake with an interchange of Chapters 4 and 5 occurs in the table of contents on page IX, otherwise no obvious typographic errors have been discovered.

This beautiful monograph deserves a whole-hearted welcome as an adjunct for performing more direct examinations on the venous side of the circulation.

Ake Gullmo



Fig 3 Case 3 Angiography of the common hepatic artery 2 to 3 hours after the injury a) Arterial phase Retrograde filling of portal vein ( $\rightarrow$ ) through arteriovenous fistula b) Three seconds later Distinct retrograde filling of portal vein ( $\rightarrow$ ) and filling of its peripheral branches in lower part of right lobe ( $\Rightarrow$ )

*Case 3* Boy aged 16 admitted one hour after a traffic accident, with pain in the right upper abdomen Selective angiography of the common hepatic artery (Fig 3) demonstrated an arteriovenous shunt in the right hepatic lobe transferring blood from a branch of the hepatic artery to the main stem and branches of the portal vein Arterial filling of these portal branches prevented their demonstration in the venous phase of a selective splenic angiography The treatment was conservative and the patient recovered in the course of ten days Angiography of the celiac artery three months later was normal

*Case 4* Girl aged 5 admitted seven hours after being struck in the abdomen by a hand cart Angiography of the celiac artery (Fig 4) disclosed stretched and arching arterial branches in the central part of the right hepatic lobe The circulation was considerably delayed peripherally and a large expansive process lay centrally the liver was displaced medially Laparotomy was performed and a large rupture in the central part of the liver sutured The postoperative course was uneventful Angiography of the celiac artery five months later demonstrated some displacement and crowding of arterial branches in the area around the sutured rupture

*Case 5* Boy aged 8 fell off his bicycle onto the handlebars Nine days later he collapsed but laparotomy failed to reveal any hepatic rupture During the following seven weeks the boy had repeated colic transient jaundice as well as haematemesis and melena, indicative of haemobilia Two subsequent laparotomies failed to reveal the arteriovenous



Fig 1



Fig 2a



Fig 2b

Fig 1 Case 1 Angiography of the celiac artery 12 days after injury. Bile beneath the right hemidiaphragm and in the right flank. Displacement and occlusion of one artery in the right hepatic lobe ( $\rightarrow$ ). Minor pseudoaneurysms ( $\leftrightarrow$ ) and early filling of portal vein branches ( $\leftrightarrow$ ) indicating arteriovenous fistula.

Fig 2 Case 2 Angiography of the celiac artery a few hours after the injury. a) Delayed filling of branches in the lower portion of the right hepatic lobe ( $\rightarrow$ ). b) Seven seconds later. Prolonged filling of branches in the lower part of the lobe ( $\rightarrow$ ).

Angiography has been performed in nine cases of hepatic rupture in our departments in the course of the last five years. In eight of these the angiographic signs were positive while no abnormality was detected in the remaining case.

### Case reports

*Case 1* Male, aged 27, admitted a few hours after a traffic accident in which a steering wheel had been forced against his abdomen. Splenectomy was performed for rupture of the spleen, and a rupture in the posterior part of the right hepatic lobe was sutured. Recurrent pain in the right hypochondrium at twelve days suggested angiography of the celiac artery (Fig 1). This revealed an avascular zone beneath the right hemidiaphragm and in the right flank produced by an accumulation of fluid. A hypovascular zone was evident in the right hepatic lobe and an occlusion was present in an artery running into this area. Minor pseudoaneurysms and early filling of portal radicles indicating the presence of arteriovenous shunts were apparent. Delayed emptying of an arterial branch was also observed, possibly referable to contusion with edema causing increased resistance to the flow by vascular compression. Three liters of fluid, looking like bile, were collected from the upper abdomen through a minor incision. Some pleural fluid was collected by repeated punctures during the following days. The patient recovered in the course of five weeks.

*Case 2* Male, aged 73, admitted a few hours after a traffic accident in which he had been hit in the chest by a steering wheel. Angiography of the celiac artery (Fig 2) revealed considerably delayed circulation in the right hepatic lobe, particularly in its lower part. This was considered to be due to hepatic contusion with edema causing vascular compression, and operation was considered unnecessary. Fluid in the right pleural cavity was removed by puncture. The patient recovered in the course of four weeks.

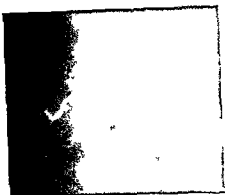


Fig 6 Case 6 Angiography of the celiac artery two years after operation for a central cyst of the liver. Filling of portal vein branches in right lobe through arteriovenous fistula (→)

fistula. Angiography of the celiac artery (Fig 5) three months after the injury disclosed a pseudoaneurysm and arteriovenous fistula of the right hepatic lobe. The abdomen was opened and the fistula located in accordance with the angiographic findings. The fistula was excised, but the right hepatic artery had to be ligated to stop the bleeding. The subsequent course was uneventful.

**Case 6** Female, aged 67, admitted for gastrointestinal bleeding, had been operated upon two years previously for a cyst in the left hepatic lobe. Benzidine tests of the stools had been persistently positive during the previous six months. Percutaneous splenic phlebography disclosed considerable dilatation of the splenic and portal veins, but no collateral circulation; the splenic pulp pressure was elevated (60 cm of water). Angiography of the celiac artery (Fig 6) revealed filling of portal vein branches through an arteriovenous fistula in the lateral part of the right hepatic lobe. Laparotomy failed to disclose the source of the bleeding. Following further continuous bleeding for a few days the patient gradually recovered.

**Case 7** Male, aged 70, admitted for jaundice and possible tumour of the liver. At laparotomy no malignancy was detected, and biopsy revealed cholangitis. The liver became considerably enlarged during the postoperative period. Angiography of the celiac artery (Fig 7) two months later revealed that the hepatic artery was displaced to the left, some branches arched around a large expansive process in the right hepatic lobe. The liver parenchyma was displaced medially. Four liters of green fluid were aspirated by percutaneous puncture. Recovery was uneventful.

**Case 8** Boy, aged 12, run over by a school bus. A deep open rupture in the right hepatic lobe was sutured. During the subsequent three weeks he was reoperated upon twice for further haemorrhage. At four weeks he was readmitted for persistent bleeding through the drainage opening. Selective angiography of the common hepatic artery (Fig 8), demonstrated stretched and arching arterial branches, and defects centrally in the right hepatic lobe. The liver was displaced medially. Further laparotomy revealed a large haematoma in the lobe and bleeding from the sutured rupture. The anterior part of the lobe was removed. Three days later, because of persistent bleeding, the entire right lobe was resected. The loss of blood however continued and the patient died ten days later.



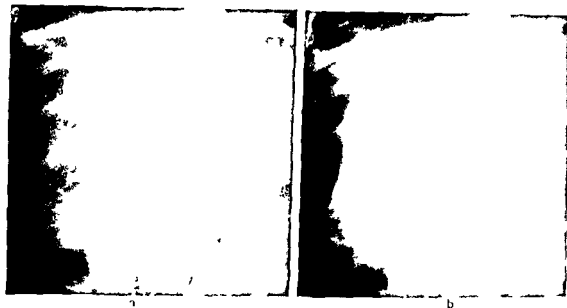


Fig 4 Case 4 Angiography of the celiac artery 8 to 9 hours after the injury a) Arterial phase Stretched branches and vascular zone centrally in right lobe corresponding to large haematoma b) Early parenchymal phase Delayed circulation in periphery of right lobe Medial displacement of liver



Fig 5 Case 5 Angiography of the celiac artery 3 months after the injury a) Arterial phase Filling of a pseudoaneurysm in upper part of right lobe b) Parenchymal phase The pseudoaneurysm drains into the bile ducts (→) (Reproduced from Brit J Radiol 41 (1968) 789)

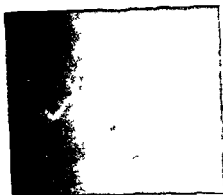


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Fig 7 Case 7 Angiography of the celiac artery two months after liver biopsy at operation a) Arterial phase Hepatic artery branches crowded medially, some of them arching around a large subcapsular hematoma in the right lobe b) Parenchymal phase Considerable medial displacement of parenchyma (→)

Fig 8 Case 8 Angiography of the common hepatic artery at four weeks and following suture of hepatic rupture Stretched and arching hepatic artery branches with defects laterally in the right hepatic lobe (→) Medial displacement of cystic and gastroduodenal arteries fluid in the right flank displacing the liver medially



### Comments

The true extent and type of hepatic trauma can hardly be assessed at operation, as experienced in 3 of the present cases and stressed by previous investigators (MILLS 1961, SOLHEIM 1963). The complicated anatomy of the liver implies that different types of damage may be expected. The most serious threat is represented by bleeding from rupture of major vessels. Large portal and hepatic

Table  
*Angiographic findings in hepatic rupture*

| Case number                      | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 |
|----------------------------------|---|---|---|---|---|---|---|---|
| Displaced arteries               | + | 0 | 0 | + | 0 | 0 | + | + |
| Occluded arteries                | + | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Extravasation of contrast medium | + | 0 | 0 | 0 | + | 0 | 0 | 0 |
| Delayed circulation              | + | + | 0 | + | + | 0 | 0 | + |
| Arteriovenous fistula            | + | 0 | + | 0 | 0 | + | 0 | 0 |
| Arterioportal fistula            | 0 | 0 | 0 | 0 | + | 0 | 0 | 0 |
| Expansive processes              | 0 | 0 | 0 | + | 0 | 0 | + | + |
| Displacement of the liver        | + | 0 | 0 | + | 0 | 0 | + | + |

vein radicles as well as hepatic artery branches in the liver may be torn and result in profuse bleeding. This may result in large intrahepatic haematomas, or, if communication is established with the bile ducts, haemorrhage may take place into these and elicit haematemesis and melaena, major haemorrhage may take place into the abdominal cavity through open rupture. Rupture of major vessels coursing into the liver (portal vein and hepatic artery) or out of the liver (hepatic veins) may rapidly produce fatal haemorrhage. Associated rupture of arteries and veins in the liver may establish a fistula between hepatic artery branches and portal or hepatic vein branches.

Rupture of the bile ducts may result in leakage of bile into the peritoneal cavity and bile peritonitis. Associated rupture of bile ducts and arteries may result in arterioportal fistula and traumatic haemobilia. Occlusion of injured arteries may produce infarction. Contusion of the hepatic parenchyma may result in diffuse haemorrhage and edema of varying degree and extent. Injury of the gallbladder is rare. Rupture of the cystic artery may occur in this condition (PENN 1962). The wide spectrum of injuries is reflected in the varied angiographic findings in the present series (Table).

Displacement of arteries around expanding haematomas occurred in four instances. Similar findings may be expected when bile cysts have formed. Arterial occlusion was evident in one case and extravasation of contrast medium from ruptured arteries in two cases. This last appeared as small accumulations of contrast medium in one, and as one large pseudoaneurysm in the other case. Delayed circulation evident as prolonged filling of the arteries in localized areas was present in five cases. This may be considered as attributable to haematomas and edema compressing minor vessels. An arteriovenous fistula between hepatic artery and portal vein branches was evident in three cases. This appeared as

early filling of typical portal vein branches, and in one case by retrograde filling of the main stem of the portal vein as well. In the latter case the presence of a fistula was the more obvious in so much as the filling of the portal branches was obtained in a selective hepatic angiography, in which their filling is normally not obtained. No venous filling was obtained of these branches at selective splenic angiography in this case. Dilatation of the splenic and portal veins and increased splenic pulp pressure were evident at splenic phlebography in one case. Traumatic arteriovenous fistula between hepatic artery and hepatic vein branches may be expected to occur, but were not encountered in this series.

An arteriobiliary fistula was present in one case and filling of a large cavity leaking into the biliary ducts was detected. The demonstration of arteriovenous and arteriobiliary fistulae and haemorrhage, may be expected to vary with time, depending upon the size of the vascular rupture, the pressure of the haematoma, and the natural haemostasis. Expansive processes attributable to haematomas were evident in three cases. Displacement of the liver by intraperitoneal fluid occurred in three cases, and in another case a considerable displacement of vessels and hepatic parenchyma of the right lobe was produced by a large subcapsular haematoma.

No angiographic abnormalities were apparent in one case with rupture of the right lobe.

It is typical of hepatic trauma that even in this small material the angiographic findings varied considerably.

Late complications may occur following hepatic rupture as well as after operations in which intrahepatic lesions have been missed. A minor haematoma may gradually enlarge and result in severe complications, days or weeks later it may rupture into the peritoneal cavity (MILLS 1961) or biliary tree (SANDBLOM 1948, WHIFLAN & GILLFSPIE 1965). Again it may become infected and develop into an abscess. Traumatic bile cysts may gradually expand and eventually rupture into the peritoneal cavity. Infarction with necrosis of vessels may probably also result in haemorrhage. Some of these complications may be avoided by accurate preoperative diagnosis, preferably by angiography, but they also imply that a repeat angiography must be considered, particularly if the postoperative course is not satisfactory.

The liver is commonly given as the third organ to rupture in blunt abdominal trauma, being preceded by the kidneys and the spleen in that order (CLARK 1954, SOLHEIM 1963). In some series the liver appears to be equally frequently or more frequently damaged than the spleen (VANCE 1928, ALLEN 1931, MILLS 1961). The mortality in hepatic rupture is extremely high, and exceeds that in rupture of the kidneys and the spleen. GLENN (1956) estimated that a third of the cases will die almost instantaneously, a third within six hours of the

injury, and the remainder will survive. Hepatic rupture is usually caused by major blunt or penetrating abdominal trauma. It should, however, be noted that in cases with minor trauma rupture may result when the liver is enlarged (MILLS 1961), spontaneous rupture of the liver has been reported in pregnancy (SANES & KAMINSKI 1946).

The massive haemorrhage and shock that may occur often indicate immediate life saving surgery. Roentgen examination is therefore often not performed. It should, however, be borne in mind that the period of preoperative preparation may be utilized for angiography. The examination can ordinarily be accomplished in the course of less than an hour in the hands of trained personnel. It should further be noted that angiography may be performed successively of the kidneys, the spleen, and the liver in the same procedure. This is of essential import as multiple injuries are frequent and associated with a higher mortality rate than rupture of one single organ.

The type and extent of the lesion in hepatic rupture will probably be revealed by angiography. Significant ruptures, not detectable by angiography, may however occur as in one of the cases of the present material.

## SUMMARY

Angiography was performed in 9 cases of hepatic rupture and in all but one case revealed the condition. The angiographic signs are described and discussed against the background of the wide spectrum of hepatic trauma. The ability of the method to demonstrate signs of rupture of the liver as well as associated injuries of the kidneys and the spleen is stressed.

## ZUSAMMENFASSUNG

Eine Angiographie wurde in 9 Fällen einer Ruptur der Leber durchgeführt. Ausser in ein in Fall wurde der Zustand entdeckt. Die angiographischen Zeichen werden beschrieben und im Hinblick auf das breite Spektrum der Leber Traumata besprochen. Die Brauchbarkeit der Methode Zeichen von Leberruptur wie auch damit verbundenen Schädigungen der Nieren und der Milz nachzuweisen wird betont.

## RÉSUMÉ

Les auteurs ont fait une angiographie dans 9 cas de rupture du foie. Dans tous les cas sauf un cet examen a donné le diagnostic. Les auteurs décrivent les signes angiographiques de la rupture hépatique et étudient son diagnostic différentiel par rapport au large spectre des traumatismes hépatiques. Ils insistent sur le fait que cette méthode permet de mettre en évidence des signes de rupture du foie ainsi que des lésions associées des reins et de la rate.

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## ANGIOGRAPHY IN HEPATIC RUPTURE

by

E BOIJSEN, J KAUDE and U TYLEN

Blunt abdominal trauma may result in injury to the liver the extent and degree of which may be difficult to estimate from the clinical signs alone. Conventional radiography of the chest and abdomen may provide indirect evidence of liver rupture, detailed information concerning which will however demand selective hepatic angiography (BOIJSEN *et coll* 1966). Our first report on angiography in five patients with hepatic lesions secondary to trauma has been followed by a few papers stressing the importance of the method in the immediate post-traumatic period (FREEARK *et coll* 1968, REDMAN *et coll* 1969). Several case reports have been presented in which angiography was the only diagnostic means that made it possible to treat correctly late complications of hepatic trauma, usually hemobilia or vascular lesions (BREMER & DOWLI 1966, FOWLER & HILLER 1967, GUNDERSEN & GREEN 1967, HERMAN & HOERR 1967, ENGE *et coll* 1968, KAUDE *et coll* 1969, KATZ & MENG 1970).

The present investigation was performed in order to analyse the angiographic findings in 25 patients with liver damage and demonstrate the significance of

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Table

*Angiographic findings in 25 patients with trauma of the liver*

|  | Time interval between trauma and angiography |                      |                        |                        |                        |
|--|--|----------------------|------------------------|------------------------|------------------------|
|  | Group I<br>2-24 hours                        | Group II<br>1-7 days | Group III<br>8-14 days | Group IV<br>15-30 days | Group V<br>31-150 days |
| Number of angiographies                          | 6  | 7                    | 7                      | 10                     | 9                      |
| Findings   |  |                      |                        |                        |                        |
| Extravasation                                    | 4  | 5                    | 3                      | 2                      | 0                      |
| Arterial constrictions                           | 1  | 0                    | 0                      | 0                      | 0                      |
| Displacement of arteries<br>or veins by hematoma | 4  | 5                    | 6                      | 9                      | 2                      |
| Arteriportal shunting,<br>peripheral             | 4  | 3                    | 1                      | 3                      | 0                      |
| Arteriportal shunting,<br>central                | 0  | 0                    | 1                      | 0                      | 2 <sup>1</sup>         |
| Occlusion of arteries                            | 1  | 1 <sup>1</sup>       | 1 <sup>1</sup>         | 2 <sup>1,2</sup>       | 4 <sup>1</sup>         |
| Occlusion of portal veins                        | 0  | 1                    | 0                      | 0                      | 1                      |
| Aneurysm formation                               | 0  | 0                    | 1                      | 2                      | 3 <sup>1</sup>         |
| Liver enlarged                                   | 2  | 2                    | 7                      | 5                      | 2 <sup>1</sup>         |
| Displacement of liver                            | 4  | 3                    | 5                      | 3                      | 0                      |
| Capsular rupture                                 | 2  | 0                    | 2                      | 0                      | 0                      |

<sup>1</sup> One patient examined twice in this period<sup>2</sup> The same patient examined three times<sup>3</sup> The same patient examined once in period III, once in period IV, and twice in period V

various angiographic signs in the early as well as in the late posttraumatic period in patients subjected to operation or treated conservatively.

**Material and Methods** Twenty-five patients with liver damage were examined by angiography some hours up to 150 days following blunt abdominal trauma, this in one patient was combined with a perforating lesion. Angiography in 11 patients was repeated at 10 to 150 days either to determine the cause of late complications, which included fever, jaundice, gastro intestinal bleeding or hemobilia, or to control the course of a previously diagnosed hepatic injury. Angiography was repeated twice in one of these patients, and in another three times. A total of 39 angiographic investigations was thus performed.

Hepatic, celiac or superior mesenteric angiographies were carried out in all patients by the percutaneous catheterization technique. Usually 40 to 50 ml Isopaque Coronar were injected in adults at a rate of 10 to 12 ml/s. One to 1.5 ml/kg body weight was the dose in children. Films were exposed at a rate of 2 films/s for 4 s, 1 film/s for the following 4 s and then 1 film every other second

or 8 s. Serial angiography was performed in a p projection and supplemented if necessary with a projection that varied with the site of the trauma and the findings obtained in the first series

Nephroangiography was carried out in 11 patients because of clinical evidence of a concomitant renal injury

Fourteen patients were operated upon and the angiographic findings compared with the surgical findings

### Results

The angiographic findings are presented in the Table. The material was divided into 5 groups in order to define which angiographic findings were most frequently present within a certain period of time after the trauma. Six patients were examined within 24 hours and 7 within one to seven days, 7 were examined during the second week including 2 patients who were examined a second time because of blood loss and as a control of a severe lesion, respectively. Ten patients were examined within 15 to 30 days after the trauma. 5 of these for the first time, and 5 patients to control the course of a previously diagnosed lesion. Nine examinations were performed more than one month but under five months following the injury. All but two examinations were controls in previously operated or conservatively treated patients without evidence remaining of hepatic signs. Several vascular lesions were frequently present in one and the same patient. The lesions observed at angiography were located in the right lobe or intermediate part of the liver in 23 patients while the left lobe was involved in only 2 patients.

Extravasation of contrast medium indicating vascular lesions was the most common finding in the early posttraumatic period. Two patients examined within a few hours following trauma failed to present any evidence of extravasation. The angiography was regarded as normal in one of these, the patient was operated upon because of severe abdominal pain. Two small capsular ruptures were evident in the left lobe of the liver but no active bleeding and only a small amount of blood lay in the abdominal cavity. The second patient with no extravasation had marked localized constrictions of the extra- and intrahepatic arterial branches. At operation small infiltrates were observed on the surface of the liver but no signs of rupture were present (Fig 1).

Extravasation was usually most marked in patients examined within 24 hours after trauma (Figs 2 and 3), it was also frequent in the remaining 7 patients examined within a week following the injury (Figs 4, 5, 6). Extravasation was observed as late as 21 days after trauma in two patients.



Fig 1 Celiac angiography in a 50 year old man two hours after trauma. Multiple constrictions of hepatic artery branches probably caused by spasm secondary to release of vasoconstrictors. No rupture was evident at operation but several small areas on the liver surface, harder than the surrounding parenchyma were palpated.

Eight of the 11 patients subjected to repeat angiography had had extravasation at the first examination, all within 10 days following the trauma. One of these patients, reexamined 10 days after trauma, still had extravasation, in the remaining 7 patients, reexamined 14 to 60 days following the injury, the extravasation of contrast medium had disappeared (Figs 3, 4, 5, 6).

Displacement of branches of the hepatic artery and portal vein surrounding an avascular lesion were characteristic findings with a hematoma lying in the parenchyma, or with a subcapsular hematoma. These signs were frequently observed in the acute stage (Figs 2, 3), a hematoma might, however, persist for a month after the trauma.

Eight patients with hematomas were not operated upon but controlled later by angiography and in 4 of these the hematoma had disappeared. In one patient it had decreased in size and in one, reexamined 10 days after the trauma, it had grown larger. In one patient reexamined twice the hematoma first increased in size (14 days following the trauma) but after another fortnight its size had



Fig 2 Celiac angiography in a 35 year old woman a few hours after traffic accident. Arterial (a) and venous (b) phase. Medial displacement of liver by intraabdominal hemorrhage. The lower part of the right hepatic lobe is lacerated, capsular rupture present (→). Occlusion of intrahepatic arteries (→→) displacement of vessels, extravasation and arterioportal shunting evident. The lower part of the right lobe was resected.

considerably decreased (Figs 4, 5). In another patient reexamined three times the size of the hematoma remained unchanged for thirty days, was smaller three weeks later, and was barely visible at a hundred days (Figs 7, 8).

A patient with combined perforating and blunt trauma had displacement of the intrahepatic arterial and portal venous branches caused by abscess formation (Fig 9). In another patient examined for the first time at three months, displacement was produced by a calcified intrahepatic hematoma.

Two types of arteriovenous shunting of contrast medium from branches of intrahepatic arteries into the portal veins were observed. The most frequent type of shunting was present at capillary or pre-capillary level, probably in the pre-sinusoidal arterioportal connections. It was most prominent in the early post-traumatic period (Figs 2, 3) and was observed at the latest eighteen days after trauma. This type of shunting seemed to occur also after only a moderate contusion and was in one patient the sole sign of hepatic trauma. The shunting disappeared in those patients who were reexamined later (Figs 2, 3, 6, 7, 8). The second type of shunting was observed twice and occurred directly between larger



Fig 3 Woman aged 42 with trauma of the liver and rib fractures after traffic accident. Immediate operation because of signs of intraabdominal hemorrhage revealed renal rupture but no hepatic lesion. Signs of intraabdominal bleeding and hematuria continued. a) Celiac angiography 24 hours after the accident. Marked hypervascularity and extravasation in the right and intermediate part of the enlarged liver with arteriportal shunting and vascular areas due to hematoma in the upper part of the right lobe. The liver was displaced slightly medially by intraabdominal hemorrhage. Nephroangiography demonstrated a ruptured right kidney. At reoperation a few small capsular ruptures were sutured and right nephrectomy was performed. The postoperative course was uneventful and at reexamination four weeks later marked regression of the hematomas was evident (b). A 10 mm  $\times$  5 mm aneurysm was now present in the right lobe. No further control so far performed.

branches of the hepatic artery and the portal vein (Fig 10). One patient previously reported (KAUDE et coll 1969) had also an arterial aneurysm at the site of the arteriovenous fistula.

Occlusion of the intrahepatic arterial branches was observed in 4 patients. Intra- and extrahepatic arterial collateral circulations ran to the branches distal to the occlusion (Figs 2, 4, 5). In one patient an intrahepatic artery was occluded following operation (Figs 7, 8), this was probably secondary to deep sutures applied to the region of injury. Occlusion or compression of the intrahepatic portal vein branches was observed in 2 patients in the early posttraumatic period (Fig 6) and in one further patient examined for the first time five months after

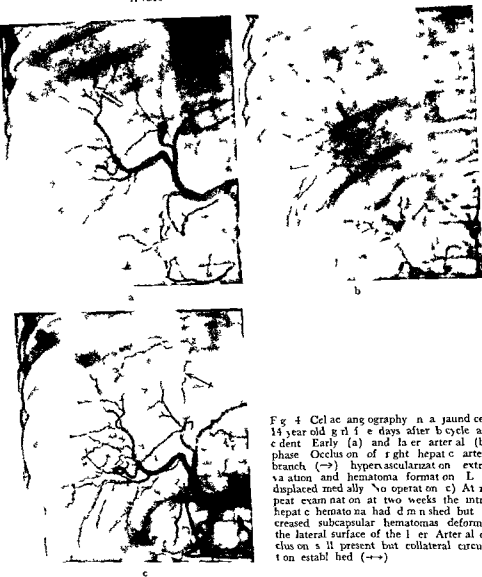


Fig 4 Celac angiography in a jaundiced 14 year old girl 5 days after bicycle accident. Early (a) and later arterial (b) phase. Occlusion of right hepatic artery branch ( $\rightarrow$ ) hypervascularization extrahepatic and hematoma formation lateral surface of liver. (c) At repeat examination at two weeks the intrahepatic hematoma had diminished but increased subcapsular hematomas deformed the lateral surface of the liver. Arterial occlusion still present but collateral circulation established ( $\leftrightarrow$ )

operation. It is possible that occlusion of portal vein branches was present in a larger number of patients but the low contrast density did not allow complete evaluation of these vessels.

An intrahepatic artery aneurysm during the first 3 weeks after trauma was observed only once. This had decreased in size at the control two months fol-

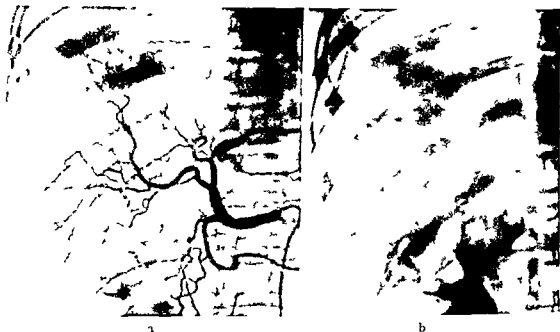


Fig 5 Same case as in fig 4 Repeat examination at four weeks Arterial (a) and capillary (b) phase Patient clinically recovered Liver then of normal size but still displaced slightly medially The hematomas had diminished in size collateral circulation to the occluded artery still present

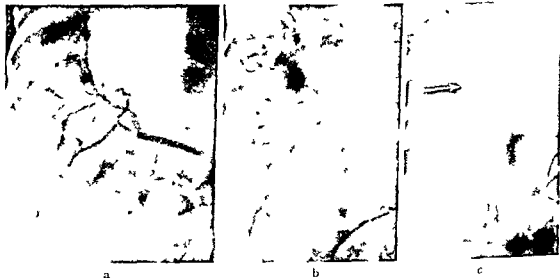


Fig 6 Hemobilia in a 7 year old girl after traffic accident Superior mesenteric angiography at seven days Arterial (a) capillary (b) and venous (c) phases The right hepatic artery arose from the superior mesenteric artery right hepatic lobe hypervascular Marked extravasation and peripheral arteriportal shunting present Displacement of intrahepatic arteries due to central hematoma formation with compression of portal vein in venous phase (→) Conservative treatment with blood transfusions Repeat angiography at two months was normal

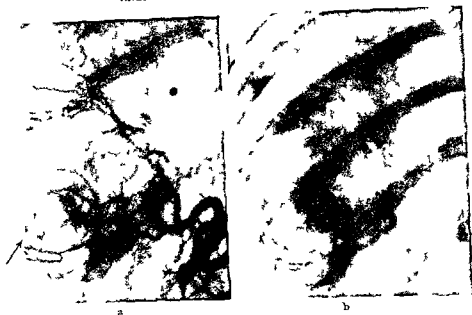


Fig 7 A 20 year old woman with cerebral contusion after traffic accident underwent

in the capillary phase

lowing the trauma (Fig 11) A 10 mm  $\times$  5 mm aneurysm in the same area had developed one month later in a patient with marked extravasation of contrast medium in the early posttraumatic period (Fig 3) Another patient with hemo- bilia at 3 weeks after trauma and suture of a laceration of the left hepatic lobe had an aneurysm 4 mm in size (Fig 12) In a fourth patient an aneurysm was observed incidentally at angiography of the kidneys 90 days following the injury, this measured 10 mm  $\times$  15 mm and was combined with an arterioportal fistula After ligation of the hepatic artery repeat angiography demonstrated that the aneurysm and the fistula were supplied via arterial collaterals but the shunting into the portal vein had considerably decreased (KAUBE et coll 1969)

The liver was frequently enlarged and hypervascular, particularly during the second to the fourth week after the trauma Livers reexamined during this period had usually increased in size but at repeat examination more than four weeks after the trauma a previously enlarged liver had always diminished in



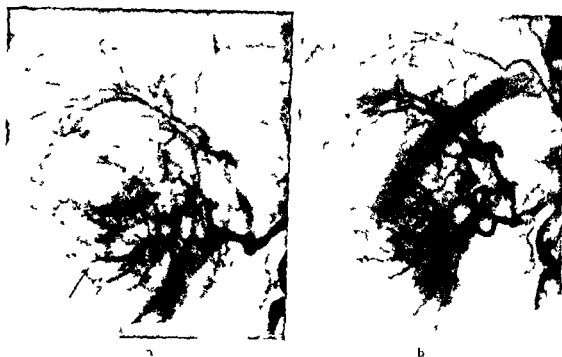


Fig 8 Same case as in fig 7 a) Repeat angiography at 30 days revealed vessel displacement unclanged and hypervascularization. The artery is now occluded ( $\rightarrow$ ) with loss of parenchyma at this site (cf fig 7 a) b) Further control at 100 days. Regression of hematoma with right hepatic lobe small and some regeneration of parenchyma

size. Hypervascularization was most prominent in those areas with arterioportal shunting or extravasation.

Displacement of the liver indicating capsular rupture with blood in the peritoneal cavity or a subcapsular hematoma was observed in 10 patients. Intra-peritoneal bleeding was indicated by medial displacement of the liver without deformation of its lateral contour unless the capsular rupture itself was demonstrated (Fig 3). Subcapsular accumulation of blood usually caused more or less marked deformation of the right lobe (Fig 9). Subcapsular and intraperitoneal hemorrhage were frequently demonstrated together (Figs 4, 5).

Concurrent splenic rupture was evident twice. Selective angiography of the right kidney was performed in 11 patients, renal rupture was disclosed in 5 of these patients.

### Discussion

Rupture of the liver is the most serious consequence of blunt abdominal trauma. Some 15 to 20 per cent of abdominal injuries involve damage of the



Fig 9

Fig 9 A 36 year old woman



Fig 10

Fig 10 Celiac angio-  
graphy. Arterioportal shunting in a 7 year old boy examined at 9 days because of progressive anemia. Conservative treatment without further control

liver (McCLELLAND & SHIRES 1965). Yet more than 50 per cent of deaths from abdominal injuries are produced by hepatic rupture (McCARROLL et coll 1962). GLENN (1956) stated that a third of those with blunt hepatic trauma may die at the scene of the accident. A third die within 6 hours and only a third survive. The mortality rate is higher in blunt hepatic trauma than in perforating injury to the liver and varies between 40 and 70 per cent (HELLSTROM 1961, SOLHEIM 1963, GLENN et coll 1966, SCHROCK et coll 1968).

It is obvious that emergency operation is usually mandatory and often life saving in hepatic rupture. This should thus not be delayed by any diagnostic procedure unless the nature of the injury is in doubt. If the clinical situation permits, acute selective hepatic angiography should be performed and the hepatic injury confirmed or excluded, since HELLSTROM (1961) has established that the mortality rate decreases with the early diagnosis of rupture. Furthermore, it has repeatedly been emphasized that it is often impossible to estimate the extent of the damage at operation, and at times the lesion cannot be found at all (SOLHEIM 1963, BRITAIN 1963). Three patients of the present series in whom no preoperative angiography was performed in the acute stage,

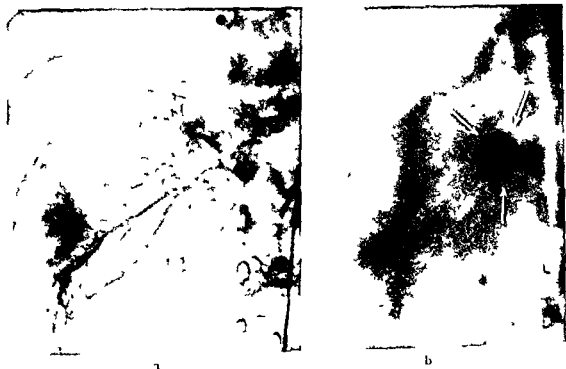


Fig. 11 A 4 year old boy operated upon because of severe abdominal bleeding a few hours after traffic accident had a 10 cm rupture on the lateral convexity of the liver which was sutured. Heavy gastrointestinal bleeding twelve days later and signs of intraabdominal fluid suggested celiac and superior mesenteric angiography. At arterial (a) and capillary (b) celiac angiography displacement of the liver and intrahepatic arteries appeared to be caused by a subphrenic and subcapsular hematoma. Furthermore an intrahepatic aneurysm 2 cm in size, was located in the hepatic hilum ( $\rightarrow$ ). At operation the hematomas were drained but the aneurysm was not removed. Repeat angiography at two months indicated that the aneurysm was 5 mm in size and the hematoma and medial displacement of the liver had disappeared.

had to be operated upon twice because the lesion was not detected nor its extent determined at the first operation (Figs 3, 7, 8, 11)

Blunt trauma of the liver may cause a variety of lesions from simple contusion without severe damage to the parenchyma to complete laceration. It may be clinically obvious that hepatic injury is present although its extent cannot be estimated. Any information that can be obtained in the acute stage will therefore be of value in planning the proper treatment.

The smaller ruptures, either located subcapsularly or centrally, are probably never diagnosed if angiography is not performed. They need no intervention and in the series of 25 patients, 11 were not operated upon despite unequivocal angiographic signs of liver damage. Not even selective angiography will always indicate rupture or contusion. It seems, however, that negative selective hepatic angiography eliminates exploration.



Fig 12 A steering wheel forced against the chest in a traffic accident produced rib fractures intraperitoneal bleeding and necessitated laparotomy in a woman aged 34. A deep rupture in the medial part of the left hepatic lobe was sutured and a choledochal T tube introduced. Ten days later a large amount of blood was drained through the tube. No further bleeding occurred. Hemoglobin normal. Celiac angiography at 21 days disclosed a 4 mm x 4 mm aneurysm (→) in the enlarged left hepatic lobe.

Gross lesions may be overlooked in aortography. FREEARK et coll (1968) reported that aortography was negative in 2 out of 5 patients with severe liver damage. The angiographic findings in the present series were positive in 13 instances of operatively verified hepatic rupture. Only in one of the 14 patients operated upon was the angiography negative. An insignificant amount of blood was present in the abdomen with two superficial capsular ruptures. Operation for liver lesion was probably not indicated at all.

Emergency operation was performed in 2 patients in both of whom hepatic damage with intraabdominal bleeding was demonstrated at angiography and confirmed. In 11 patients exploration was regarded as unnecessary because of the type and small extent of the lesion at angiography and the general good condition of the patients. Repeat angiography was performed in 5 of these, with evidence of regression of the lesion in all instances.

Several patients not included in the present series were examined by selective angiography for clinical signs of hepatic damage but because the angiographic

findings were negative, no operation was performed, it is possible that small insignificant lesions were present in some of these patients. REDMAN et coll (1969) reported apparently normal conditions at angiography in 4 out of 7 patients with hepatic trauma, which supports the impression that small lesions of little or no clinical importance are not diagnosed at angiography.

One patient of the present series was operated upon a few hours after the trauma. At preoperative angiography no evidence of a bleeding or parenchymal lesion was present. Operation disclosed only superficial, localized infiltrates that might have been related to the local vascular constrictions of branches of the hepatic artery which was the only other positive angiographic finding. Pharmacological angiography in patients examined for reasons other than hepatic trauma has occasionally revealed similar constrictions when nor-epinephrine or vasopressin was injected intraarterially in small doses (5 to 10 µg and 0.5 to 1 IU, respectively). Most probably the peripheral constrictions were secondary to a vasopressor released by the trauma and shock, and still active a few hours later when angiography was performed. Localized areas of anoxia might have caused the infiltrates observed at operation.

Extravasation of contrast medium as a result of arterial damage, arterioportal shunting of contrast medium at precapillary level by contusion, or between larger branches because of arterial rupture, as well as displacement of vessels secondary to hematoma, are the most typical signs of hepatic damage in the early post-traumatic period. Shunting to the hepatic veins as reported by REDMAN et coll (1969) was not observed. Extensive extravasation and large subcapsular and extrahepatic hematoma as signs of a capsular rupture were the main indications for operation in this early period.

Arterial occlusion is a less frequent sequela following hepatic trauma. A collateral circulation usually develops within the liver as well as via capsular arteries or from the inferior phrenic artery (KAUDE et coll 1969). In one patient with deep sutures applied in a severely traumatized part of the right hepatic lobe the collateral supply was insufficient and resulted in necrosis of a small segment. Trauma is one of the main causes of aneurysms of the hepatic artery (GUIDA & MOORE 1966) and was observed in the present series in 4 patients. With the steadily increasing number of traffic accidents trauma may soon become the most important etiologic factor in aneurysms.

One important indication for angiography in blunt abdominal trauma is thus the preoperative diagnosis and localization of the hepatic damage. The second indication is the control of the course of angiographically demonstrated lesions if no operation is performed. A third important indication for angiography is the control of operatively or conservatively treated hepatic ruptures even if no angiography had been performed preoperatively. The writers are of the opinion that

postoperative angiography should be performed in all patients whether clinical signs are present or not. Although repeat examinations in the present series demonstrated spontaneous healing of even extensive vascular lesions, late complications secondary to hepatic trauma whether operated upon or not, frequently occur and may consist of aneurysms, abscesses, biliary cysts, arteriovenous fistulae or hemobilia (SANDBLOM 1948, SWORN 1959, BRITTA 1963, GRAFF 1963, BREMER & DOWLI 1966, GLENN *et coll* 1966, GUNDERSEN & GREEN 1967, FOWLER 1967, HERMAN & HOERR 1967, ENGE *et coll* 1968, KAUDE *et coll* 1969, KATZ & MENG 1970). Several case reports and the experience of the present authors have indicated that angiography will give all the information necessary to control late complications, such sequelae may be asymptomatic for a long period of time.

It is obvious that hepatic angiography will mainly furnish information about arterial lesions. Naturally, the portal and hepatic veins as well as the bile ducts are even more vulnerable to lesions than the arteries. Splenic phlebography and cholangiography may provide further important information about hepatic rupture although the more important indications of damage to those structures will be evident from the arterial investigation.

Hemobilia, i.e. gastrointestinal bleeding via bile ducts (SANDBLOM 1948), is not an uncommon complication of hepatic trauma. The arterio-biliary fistula underlying this condition has only occasionally been demonstrated at angiography (FOWLER & HILLER 1967, ENGE *et coll* 1968). Abnormalities in the hepatic vasculature are, however, as a rule demonstrated and should direct attention to the liver as the source of the gastrointestinal bleeding. From a review by STEICHEN & SREINER (1966) it appears that hemobilia is a rare complication of hepatic injury, although it occurred three times in the present series. Arterial abnormalities were observed but the fistula itself could not be demonstrated. Hepatic vein rupture is not infrequently fatal (SCHROCK *et coll* 1968). The clinical condition of these patients requires emergency operation without previous angiography.

du  
injury. For the same reason the vascularity of the pancreas and spleen should be evaluated. Two patients of the present series had splenic rupture and in 5 patients renal damage was observed.

## SUMMARY

Selective angiography was performed in 25 patients with hepatic lesions secondary to trauma. The vascular lesions at angiography depend on the severity of the lesion and the

time interval between the trauma and the examination. The extent, site and nature of the injury may be determined. Repeat angiography to control healing should be performed when operation is not undertaken. Postoperative angiography is important to control the results of an operation.

## ZUSAMMENFASSUNG

Fünfundzwanzig Patienten mit traumatischen Leberschäden wurden mit selektiver Angiographie untersucht. Die dabei beobachteten Gefäßveränderungen sind von dem Schweregrad der Verletzung und dem Zeitabstand zwischen dem Trauma und der Untersuchung abhängig. Die Ausbreitung, Lokalisation und Natur der Verletzung können angiographisch festgestellt werden. Falls der Patient nicht operiert wird, sollte die Heilung einer diagnostizierten Verletzung angiographisch gefolgt werden. Die postoperative Angiographie ist wichtig, um das Resultat der Operation zu kontrollieren.

## RÉSUMÉ

Les auteurs ont fait une angiographie sélective chez 25 patients atteints de lésions hépatiques secondaires à un traumatisme. Les lésions vasculaires visibles par angiographie dépendent de la gravité de la lésion et de l'intervalle de temps entre le traumatisme et l'examen. L'examen permet de déterminer l'étendue, le siège et la nature de la lésion. Dans le cas où on n'intervient pas chirurgicalement, on devrait faire une nouvelle angiographie pour contrôler la guérison. Il est important de contrôler par une angiographie post-opératoire le résultat d'une opération.

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## ROENTGENOLOGIC DETERMINATION OF THE VARIATIONS IN HEART VOLUME DURING THE CARDIAC CYCLE

by

K. BERGSTROM, L. BACKLUND and U. ERIKSON

Variations in heart volume during systole and diastole have been investigated by roentgenologic methods by several authors. Contradictory results have been reported. JONSELL (1939) believed that the difference between the diastolic and systolic volumes could amount to about 20 per cent of the diastolic value, but that the usual difference obtained in determinations in young adults was about 15 per cent. HUBACHER & NYLFEIER (1946) also recorded a difference between the diastolic and systolic volumes and suggested the use of this difference for the calculation of the stroke volume. LIND (1950) observed in a series of 18 children that the variations in the heart volume during the cardiac cycle could be as great as 10 to 15 per cent of the mean heart volume.

The diastolic volume was usually the greater but the systolic was sometimes more than or equal to the diastolic volume. KJELLBERG et coll (1951) recorded no statistically significant difference between the cardiac volume during systole and diastole. HALI et coll (1961) considered this difference to be small (not

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more than 10 per cent) Tachycardia often obscured the variation EVANS & CARPENTER (1965) reported that the estimated diastolic systolic variation was significant only for normal hearts This suggested an investigation of the problem by serial angiography in a number of patients with cardiac diseases and by serial radiography in a series of healthy subjects

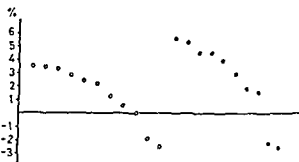
*Material* A total of 21 subjects 10 of them patients with cardiac disease, were investigated One woman aged 25, had aortic insufficiency and one, aged 47, had mitral and aortic stenosis Seven men out of 8, aged 21 to 61, had aortic insufficiency and one aortic stenosis The diagnoses were confirmed by angiocardiology and cardiac catheterization The other 11 were healthy volunteers, students 20 to 25 years of age, 2 of them were women and 9 were men They were of ordinary physical status and had a normal ECG at rest and during exercise and normal physical working capacity (determined by bicycle ergometry)

*Methods* The cardiac patients were investigated by a routine programme with a view to possible operation Serial angiocardiology was performed with a two plane automatic film changer at a frequency of six frames per second for three seconds followed by one frame per second for 10 seconds, the FFD was 80 cm and the exposures and the ECG were recorded by a direct ink recorder The contrast medium in 9 patients was injected into the left atrium via a trans-septal catheter thoracic aortography was performed in one patient with severe aortic insufficiency

The healthy volunteers were also investigated by means of the two-plane film changer and the exposures and ECG recorded by the direct ink recorder, but no contrast medium was injected All subjects were investigated in the supine position with the central beams at right angles to the film planes Exposures were made during superficial breathing

The angiocardiology of the patients were evaluated as to total heart volume in relation to the ECG The smallest systolic volume and the largest diastolic volume were chosen The heart volumes for the healthy volunteers were measured at the end of the T wave in the ECG for the end systolic phase and at the P wave for the end diastolic phase Three diameters were used in accordance with the recommendations of JONSELL (1939) The volume  $V$  was obtained by  $V = k \cdot abc$  where  $k$  is a constant and  $a$   $b$  and  $c$  the diameters At least two volumes in each phase of the cardiac cycle were measured The diastolic volume was taken as 100 per cent with the systolic volume expressed in the relative term Volumes in other phases of the cardiac cycle were also measured to obtain further information

The relative difference (as percentage of the diastolic volume) between the end diastolic and the end systolic volumes of each subjects arranged in order of decreasing difference. Open circles represent healthy volunteers and filled circles cardiac patients.



## Results

The difference between the end-diastolic and end-systolic heart volumes is given in the figure for each subject investigated. The diastolic volumes were somewhat greater than the systolic volumes in 8 of the 10 cardiac patients and in 8 of the 11 healthy volunteers, the highest individual difference was 5.7 per cent. The average values were 2.6 and 1.4 per cent, respectively. The pulse rates at the times of the measurements were between 60 and 80 per minute.

The volumes obtained for other phases of the cardiac cycle varied less than the end-diastolic or end-systolic volumes.

Calculation of the error of a single determination indicated no significant differences between two randomly chosen diastolic volumes or two systolic volumes. The coefficients of variation for the total material were for the volumes in diastole and systole 2.5 and 2.7 per cent, respectively. The differences between the diastolic and the systolic volumes in two pairs of exposures were not significant for the healthy group. The patients with cardiac diseases had in the first pair of exposures as a mean a diastolic volume 4.5 ml larger than the systolic volume ( $p=0.01$ ,  $t=3.66$ ) and in second pair 6.4 ml ( $p=0.05$ ,  $t=2.26$ ), respectively.

The results indicate a negligible or very small difference between the end-diastolic and end-systolic volumes of the total heart in the supine body position. For the cardiac patients however, there were significant differences although in absolute figures they were small. This finding is in accordance with the result of KJELBERG *et coll.* (1951) who in five groups of mostly men recorded no statistically significant change in the cardiac volume during systole or diastole. They also observed no increase in error or difference on deep inspiration. This held for both the prone and the sitting positions and for single exposures, i.e. no serial exposures were made. Very small differences between the diastolic and systolic heart volumes have also been recorded in the upright position (cf. KLEPZIG & FRISCH 1965). LIND (1950) made double determinations in systole and diastole in 18 infants and demonstrated significant differences. Another 5 patients were investigated (LIND) by synchronous serial radiography in two planes at right

angles and in this series the variations in the roentgenologic heart volume were as great as 10 to 15 per cent of the mean heart volume. As in the present investigation however, LIND observed that the systolic volume was greater than or equal to the diastolic volume and, like KJELLBERG et coll (1951), exposures on inspiration or expiration revealed no significant differences in the volumes. EVANS & CARPENTER (1965) noted a mean decrease in the heart volume during systole which was highly significant for normal hearts, and a mean decrease which was not significant for abnormal hearts. They used a technique essentially similar to that of JONSELL (1939), that is with the patient in the upright position.

HALL et coll (1961) in an investigation of 150 patients in the standing position stated that the differences between systolic and diastolic heart volumes were not more than 10 per cent, with variations of up to 15 per cent at low heart rates, the variations were not always measurable during tachycardia. The present investigation was performed in the recumbent position, but supine as opposed to the prone position used by KJELLBERG et coll (1951), and JONSELL's formula was used. According to BERGSTROM et coll (1969), volumes calculated by means of the formulae of KJELLBERG et coll and JONSELL are in good agreement. The present results differ, however, from those of JONSELL, who recorded a difference of about 15 per cent in young healthy adults, i.e. diastole larger than systole. The technique of the two investigations also differ although this can probably not explain the lack of agreement. One explanation may be the different position since recordings in the upright, but not in the recumbent position, have usually been found to produce differences between the systolic and diastolic volumes. The standard error of a single determination is of importance, HELLSTROM & HOLMGREN (1966) reported a standard error of about 4 per cent. The coefficient of variation in the present work was about 2.6 per cent.

The normal variations in the atrial volume during the cardiac cycle have not been fully investigated (cf BRECHER & GALLETTI 1963). However, from a physiologic standpoint there is no reason to assume that large differences in the total heart volume between diastole and systole occur, because of the rapid atrial filling during ventricular systole. The relative constancy of the total heart volume during the cardiac cycle indicates that changes in ventricular and atrial volumes balance each other. The roentgenologic heart volume includes a blood volume as well as a myocardial and pericardial volume and the alternation in these two main factors is difficult to assess. The exact blood content of the atria and ventricles and the volume of the cardiac musculature cannot be measured accurately with the methods available today.

From a practical viewpoint it seems unnecessary to use an ECG trigger for simultaneous exposures when examinations are made in the horizontal body position.

## SUMMARY

The heart volume was measured in the supine position by simultaneous right angled exposures at a frequency of six frames per second recorded together with the ECG in 10 cardiac patients and 11 healthy subjects. The coefficient of variation was 2.6 per cent. The end-diastolic volume was 2.6 per cent larger than the end-systolic volume in the cardiac patients and 1.4 per cent greater in the controls.

## ZUSAMMENFASSUNG

An 10 Herzkranken und an 11 gesunden Personen wurde das Herzvolumen in Rückenlage mittels gleichzeitigen und elektrokardiographisch kontrollierten Röntgenaufnahmen in zwei Ebenen mit einer Rate von 6 Bildern pro Sekunde gemessen. Ein Variationskoeffizient von 2,6 Prozent wurde gefunden. Es zeigte sich, dass bei Herzkranken das enddiastolische Volumen 2,6 Prozent grösser war als das endsystolische Volumen. In der Kontrollgruppe war der Unterschied 1,4 Prozent.

## RÉSUMÉ

Les auteurs ont mesuré le volume cardiaque en décubitus par radiographies simultanées perpendiculaires à la fréquence de six clichés par seconde avec enregistrement simultané de l'électro-cardiogramme chez 10 cardiaques et 11 sujets sains. Le coefficient de variation est 2,6 pour cent. Le volume télédiastolique est de 2,6 pour cent plus grand que le volume télé-systolique chez les malades cardiaques et de 1,4 pour cent chez les sujets témoins.

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## EFFECT OF WATER INGESTION ON SPLEEN SIZE AS DETERMINED BY RADIOISOTOPE SCANS

by

JAMES D. PARKER and LESLIE R. BENNETT

ANDREN (1957) reported that spleen length increased one to two centimeters on abdominal films of prone normal subjects shortly after the ingestion of one liter of water. The enlargement occurred in all subjects tested and was most prominent in the younger ones. It diminished or disappeared when the subject got up and reappeared when he lay down. ANDREN believed the change in spleen size to be due to an increase in portal blood flow and pressure.

This hypothesis prompted ALMEN & ANDREN (1961) to test patients with hepatocellular or obstructive jaundice. They reported that all of the latter and most of the former

spleen size. The investigators felt this was due to increased portal pressure which prevented further splenic enlargement after water ingestion.

This water load test of jaundice has appeared in books on roentgen diagnosis (BERANBAUM & MEYERS 1964, ROSCH 1967) and has been referred to in articles on spleen diagnosis (ROSCH 1965) and size estimation (WHITLEY et al. 1966).

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Table

*Splenic dimensions before and after ingestion of one liter of water in nine normal subjects*

| Subject | Age<br>(years) | Splenic<br>dimen-<br>sion* | Rectilinear scan   |                         |                          |                          |
|---------|----------------|----------------------------|--------------------|-------------------------|--------------------------|--------------------------|
|         |                |                            | Pre in-<br>gestion | 0 min post<br>ingestion | 15 min post<br>ingestion | 30 min post<br>ingestion |
| 1       | 21             | Area                       | 81                 | 81                      |                          | 80                       |
|         |                | Length                     | 13.3               | 13.2                    | —                        | 13.0                     |
|         |                | Width                      | 8.0                | 8.0                     |                          | 7.5                      |
| 2       | 21             | Area                       | 90                 | 91                      |                          | 86                       |
|         |                | Length                     | 13.2               | 13.2                    | —                        | 13.2                     |
|         |                | Width                      | 8.4                | 8.4                     |                          | 8.2                      |
| 3       | 23             | Area                       | 88                 | 76                      |                          | 84                       |
|         |                | Length                     | 13.3               | 13.1                    | —                        | 13.2                     |
|         |                | Width                      | 8.2                | 7.3                     |                          | 7.9                      |
| 4       | 23             | Area                       | 61                 | 71                      |                          | 64                       |
|         |                | Length                     | 10.8               | 11.6                    | —                        | 11.5                     |
|         |                | Width                      | 6.2                | 6.6                     |                          | 6.8                      |
| 5       | 21             | Area                       | 76                 |                         | 80                       | 76                       |
|         |                | Length                     | 11.4               | —                       | 14.1                     | 14.6                     |
|         |                | Width                      | 6.4                |                         | 7.2                      | 6.4                      |
| 6       | 21             | Area                       | 106                |                         | 109                      | 108                      |
|         |                | Length                     | 14.0               | —                       | 14.1                     | 14.2                     |
|         |                | Width                      | 9.9                |                         | 10.0                     | 9.8                      |
| 7       | 25             | Area                       | 106                |                         | 107                      | 110                      |
|         |                | Length                     | 14.4               | —                       | 15.0                     | 15.0                     |
|         |                | Width                      | 9.2                |                         | 9.2                      | 9.6                      |
| 8       | 23             | Area                       | 67                 |                         | 66                       | 60                       |
|         |                | Length                     | 10.0               | —                       | 10.0                     | 9.7                      |
|         |                | Width                      | 8.3                |                         | 8.5                      | 8.4                      |
| 9       | 23             | Area                       | 91                 |                         | 88                       | 94                       |
|         |                | Length                     | 13.4               | —                       | 12.3                     | 13.0                     |
|         |                | Width                      | 9.0                |                         | 9.2                      | 9.2                      |

\* Area in cm<sup>2</sup>, length and width in cm

Because of the importance of the observation for the determination of spleen size by abdominal film or radioisotope scan we made the following investigation. The results indicate that the observed change in spleen size is due mainly to change in spleen position.

**Materials and Methods** After overnight fasts and on different days, nine normal young male volunteers were each given two mCi of technetium 99m sulfur colloid intravenously. All underwent supine rectilinear liver-spleen scans. A dual probe Ohio-Nuclear model 54 scanner equipped with 5 inch crystals and 85-hole fine focus collimators was used. The scanning speed was 400 cm/min.

Table (cont)

| Camera scan              |                            |                         |                           |
|--------------------------|----------------------------|-------------------------|---------------------------|
| Pre ingestion<br>sitting | Post ingestion,<br>sitting | Pre ingestion<br>supine | Post ingestion,<br>supine |
| —                        | —                          | —                       | —                         |
| —                        | —                          | —                       | —                         |
| —                        | —                          | —                       | —                         |
| —                        | —                          | —                       | —                         |
| 43                       | 46                         | 48                      | 47                        |
| 10.9                     | 11.4                       | 11.2                    | 12.2                      |
| 4.5                      | 4.6                        | 5.6                     | 5.4                       |
| 56                       | 65                         | 58                      | 69                        |
| 10.0                     | 10.7                       | 10.8                    | 11.2                      |
| 6.8                      | 7.2                        | 7.2                     | 7.9                       |
| 59                       | 60                         | 56                      | 68                        |
| 10.8                     | 10.8                       | 10.3                    | 11.6                      |
| 6.6                      | 7.2                        | 6.6                     | 7.4                       |
| 32                       | 34                         | 38                      | 36                        |
| 7.6                      | 7.6                        | 7.8                     | 7.4                       |
| 5.2                      | 5.7                        | 6.4                     | 7.0                       |
| 42                       | 48                         | 50                      | 54                        |
| 9.0                      | 9.2                        | 10.0                    | 9.8                       |
| 5.5                      | 6.8                        | 6.3                     | 7.0                       |

Each scan took about fifteen minutes. Film light intensity and count rate were the same for all subjects and scans. Count rate was kept constant by window adjustment. The distances from the collimator faces to the table top were the same for all the scans of each individual.

After completion of the first scan four subjects drank one liter of tap water and were re-scanned immediately and thirty minutes afterwards in the supine position only. The remaining five subjects underwent posterior spleen scans in the sitting, then in the supine, positions with an Anger scintillation camera (Nuclear-Chicago). For each view 400 000 counts were collected. Polaroid and



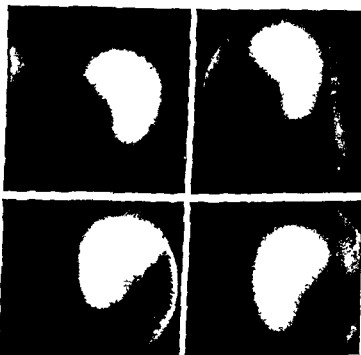


Fig 1 Subject 7 Scintillation camera posterior spleen scan Upper left Before water ingestion Subject sitting Upper right Ten minutes after water ingestion Subject sitting Lower left Before water ingestion Subject supine Lower right Five minutes after water ingestion Subject supine

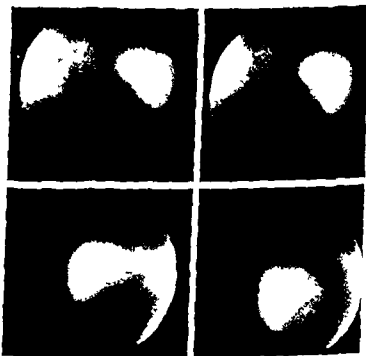


Fig 2 Subject 8 Scintillation camera posterior spleen scan Upper left Before water ingestion Subject sitting Upper right Ten minutes after water ingestion Subject sitting Lower left Before water ingestion Subject supine Lower right Five minutes after water ingestion Subject supine

eleven by fourteen inch (28 cm  $\times$  35.5 cm) films were obtained simultaneously. Film light intensity was the same for all the scans. Each scan took about five minutes. Following the first two camera scans, the five subjects each drank one



Fig 3 Subject 4 Rectil near posterior liver spleen scan Left Before water ingestion The spleen is on the right Right Immediately after water ingest on The spleen has moved down and its diaphragmatic end has been pushed laterally

liter of water and were re scanned in the supine, then in the sitting, positions. Finally, they underwent rectilinear scanning, in the supine position only, fifteen and thirty minutes after fluid ingestion.

Spleen area was measured by planimetry on the posterior rectilinear scans and the eleven by fourteen inch camera scans. Maximum spleen length and maximum width perpendicular to the length were also measured. Subjects' names were concealed by tape and the films were then numbered and mixed using a table of random numbers. Measurements were made independently by the two investigators and the results were averaged.

## Results

Spleen measurements for the scans of the nine subjects are given in the Table. Of the four subjects who underwent rectilinear scanning alone, two showed a five per cent or less change in spleen area. One subject (No 3) showed a fourteen per cent decrease in area on the scan done immediately after water ingestion and another (No 4) showed a sixteen per cent increase in area.

Of the five who underwent rectilinear and camera scanning, four (Nos 5, 6, 7, 9) showed a six per cent or less change in spleen area on the rectilinear scans. Three of these (Nos 6, 7, 9), however, showed increases in area on both the sitting and supine camera scans. The camera scans of one of these subjects (No 7) are shown in Fig 1. Spleen area increased 21 per cent in the supine position. The fifth subject (No 8) showed a ten per cent decrease in area on the thirty minute rectilinear scan but had no remarkable change in area on the camera scans although there was a striking change in spleen configuration in the supine position (Fig 2). Spleen length decreased and width increased, making the organ triangular in shape.

In most subjects the spleen was pushed laterally and away from the head by the stomach. This is well shown by the rectilinear scans of subject No 4 in Fig

3 The spleen was pushed down in relation to the liver and its diaphragmatic end was moved laterally. Concomitant with this shift in position, spleen area increased sixteen per cent.

### Discussion

Although portal blood flow and pressure were not measured in this investigation, or, for that matter, in the investigations of ANDRÉN (1957) and of ALMÉN & ANDRÉN (1961), we feel that the observed changes in spleen size are due mainly to changes in spleen position rather than to increased portal flow and pressure because the changes occurred too fast in our investigation (within five minutes) and those of ANDRÉN & ALMÉN (within one minute) for any significant absorption of water to have occurred. HUNT & SPURRELL (1951) have shown that about thirty minutes are required for half of a 750 ml citrus pectin and sucrose liquid meal to be emptied by the stomach. Furthermore, there is little net gastric water absorption (DAVENPORT 1966), although a single drink of one liter water is absorbed by the intestine within one hour and fifty per cent is absorbed within thirty minutes (DAVENPORT 1966).

Some of our subjects showed no change in spleen size after water ingestion or showed a decrease in area rather than an increase. Also, most of our subjects showed a change in spleen position laterally and away from the head and one showed a marked change in spleen configuration. These alterations in spleen position and shape were presumably due to pressure from the large adjacent stomach.

ANDRÉN (1957) reported a consistent increase in spleen length after water ingestion in normal subjects. This may be due to a change in spleen position on the prone p.a. abdominal film such as to lead to apparent splenic enlargement on most films. We did not attempt to verify this in our subjects by abdominal films because we wanted to keep the radiation dose as low as possible. Our scans were done in the posterior supine or sitting positions. The fact that ALMÉN & ANDRÉN (1961) found that all of their 13 patients with obstructive jaundice had an increase in spleen size while only 28 of their 46 patients with hepatocellular jaundice had such a change may be due to the small size of the former group compared with the latter.

The effect of fluid ingestion on spleen area determination, while important in the immediate post ingestion period, is apparently negligible after about thirty minutes. Rectilinear spleen areas thirty minutes after water ingestion in eight of our nine subjects were within five per cent of the pre-ingestion values. ALMÉN & ANDRÉN reported that enlargement disappeared within an hour in all their subjects.

### Acknowledgement

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### SUMMARY

Posterior spleen scans using technetium 99m sulfur colloid were performed on nine normal young male volunteers before and after the ingestion of one liter of water. Scintillation camera and rectilinear scanners were used. Variable changes in spleen size occurred after the water ingestion. In one subject spleen configuration changed markedly. In most subjects the spleen was pushed laterally and away from the head by the stomach. The rapid changes in spleen size are felt to be due to changes in spleen position rather than to increased portal flow and pressures as postulated in previous roentgenologic investigations.

### ZUSAMMENFASSUNG

Bei neun normalen männlichen freiwilligen Versuchspersonen wurden vor und nach Einnahme von einem Liter Wasser hintere Milz-Scintigramme mit einer Scintillationskammer und einem rektilinearen Skintigraphen benutzt. Es wurden variable Veränderungen der Milzgrösse nach der Wasseraufnahme beobachtet. Bei einem Versuchspersonen änderte sich die Milzform deutlich. Bei den meisten Personen war die Milz nach rechts und von der Kopfseite weg verschoben. Die raschen Änderungen der Milzgrösse beruhen offenbar mehr auf Änderungen der Lage der Milz als auf erhöhter portaler Strömung und erhöhtem Druck wie in früheren roentgenologischen Untersuchungen behauptet worden ist.

### RÉSUMÉ

Les auteurs ont fait des scintigraphies spléniques postérieures au sulfure colloïdal de technetium 99m chez neuf jeunes hommes normaux volontaires avant et après l'ingestion d'un litre d'eau. Ils ont utilisé une caméra à scintillation et un scintigraphe linéaire. L'ingestion d'eau est suivie de modifications variables des dimensions de la rate. Chez un sujet la forme de la rate a changé de façon notable. Chez la plupart des sujets la rate est repoussée en dehors et en bas par l'estomac. Les auteurs pensent que les modifications rapides des dimensions de la rate sont dues aux modifications de la position de la rate plutôt qu'à une augmentation du débit portal et de la pression comme l'avait fait penser des études radiologiques précédentes.

3 The spleen was pushed down in relation to the liver and its diaphragmatic end was moved laterally. Concomitant with this shift in position, spleen area increased sixteen per cent.

### Discussion

Although portal blood flow and pressure were not measured in this investigation, or, for that matter, in the investigations of ANDREN (1957) and of ALMEN & ANDREN (1961), we feel that the observed changes in spleen size are due mainly to changes in spleen position rather than to increased portal flow and pressure because the changes occurred too fast in our investigation (within five minutes) and those of ANDREN & ALMEN (within one minute) for any significant absorption of water to have occurred. HUNT & SPURRILL (1951) have shown that about thirty minutes are required for half of a 750 ml citrus pectin and sucrose liquid meal to be emptied by the stomach. Furthermore, there is little net gastric water absorption (DAVENPORT 1966), although a single drink of one liter water is absorbed by the intestine within one hour and fifty per cent is absorbed within thirty minutes (DAVENPORT 1966).

Some of our subjects showed no change in spleen size after water ingestion or showed a decrease in area rather than an increase. Also, most of our subjects showed a change in spleen position laterally and away from the head and one showed a marked change in spleen configuration. These alterations in spleen position and shape were presumably due to pressure from the large adjacent stomach.

ANDREN (1957) reported a consistent increase in spleen length after water ingestion in normal subjects. This may be due to a change in spleen position on the prone post abdominal film such as to lead to apparent splenic enlargement on most films. We did not attempt to verify this in our subjects by abdominal films because we wanted to keep the radiation dose as low as possible. Our scans were done in the posterior supine or sitting positions. The fact that ALMEN & ANDREN (1961) found that all of their 13 patients with obstructive jaundice had an increase in spleen size while only 28 of their 46 patients with hepatocellular jaundice had such a change may be due to the small size of the former group compared with the latter.

The effect of fluid ingestion on spleen area determination, while important in the immediate post ingestion period, is apparently negligible after about thirty minutes. Rectilinear spleen areas thirty minutes after water ingestion in eight of our nine subjects were within five per cent of the pre ingestion values. ALMEN & ANDREN reported that enlargement disappeared within an hour in all their subjects.

## VENOUS PHASE IN SPINAL CORD ANGIOGRAPHY

by

L C FRIED J L DOPPMAN and G DI CHIRO

Angiographic investigations of the spinal cord vasculature are being performed with increasing frequency in recent years. Selective angiography (DI CHIRO et coll 1967, DJINDJIAN 1969) is particularly useful for demonstrating vascular tumors and arteriovenous malformations of the spinal cord. Although the selective techniques have demonstrated the normal arterial supply, they have only seldom demonstrated the normal venous drainage of the spinal cord. This has limited the diagnostic value of selective techniques.

Experimental angiographic techniques in primates (DOPPMAN et coll 1969, DI CHIRO et coll 1970) can increase our understanding of the radiographic anatomy of human spinal cord blood vessels. The main purpose of this report is to describe the venous phase of experimental spinal cord angiography.

SCHUB & ALEXANDER (1939) and others have comprehensively described the venous systems of the human spinal cord. The venous drainage of the spinal cord does not parallel the arterial supply. While the main arterial supply is on the anterior surface of the spinal cord, the single midline posterior spinal vein is the major venous channel of the cord. It is the largest vessel on the cord surface measuring from 1 to 2 mm in diameter. The anterior spinal vein which accompanies the anterior spinal artery is considerably smaller and is occasionally

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pared. According to SAKS (1942) the diameter of the anterior spinal vein in the Rhesus monkey averages 0.1 mm in the dorsal region and 0.25 mm in the lumbar area. The diameter of the posterior spinal vein averages 0.25 mm in the dorsal region and 0.6 mm in the lumbar area. The difference in size is approximately 2.5 times in corresponding areas, and similar differences in the anterior and posterior veins of human spinal cords might be expected.

The anterior and posterior longitudinal venous systems extend most of the length of the spinal cord and are drained by a series of anterior and posterior radiculo-medullary veins which accompany the spinal roots. The posterior spinal vein can be traced from the conus medullaris to the medulla oblongata. At the conus it divides and leaves the midline, the branches eventually leave the cord surface and exit via roots of the cauda equina.

The anterior spinal vein closely parallels the anterior spinal artery, lying slightly deeper and to the side of the artery in the median sulcus.

The posterior radiculo-medullary veins are generally larger than the anterior radiculo-medullary veins and there is usually a *vena radiculo-medullaris magna* following a posterior root in the thoracolumbar region. In the Rhesus the *vena radiculo-medullaris magna* averages 0.35 mm in diameter, but several draining veins not nearly as large are also often present.

**Materials and Methods.** We used Rhesus monkeys in these investigations because of the marked similarity of the spinal cord vasculature to that of man (SAKS 1942). The animals were anesthetized with Sernylan (Parke Davis and Company, Detroit) and sodium pentobarbital. A polyethylene catheter (PE 160) was inserted into the lower thoracic or upper abdominal aorta through an incision in the femoral artery. Manual injections of methylglucamine iohalamate (Conray 60, Mallinkrodt Chemical Company, St. Louis) 2 mg/kg were performed immediately following the intra-aortic injection of levarterenol (Levophed, Winthrop Laboratories, New York). The vasopressor base was diluted in 10 ml of 5% dextrose solution and was injected into the aortic catheter at the same rate as the contrast medium. The dosage varied from 4 to 200  $\mu$ g. The animals were rotated approximately 15° to the left side in order to prevent aortic superimposition on the spinal cord blood vessels. The rotation also prevents superimposition of midline vessels on the anterior and posterior surface of the spinal cord.

The examinations were performed with a Sanchez Perez cassette changer. A 0.3 mm focal spot tube and a lucite support which provided the increased object to film distance were employed to achieve magnification (object to film distance was 50 cm and tube to film distance 100 cm). In each series 12 films were exposed at a rate of 2 per second from the moment of contrast injection. Forty examinations were performed in all.



Fig 1 Spinal cord angiography in Rhesus monkey a) Arterial phase 3 seconds after injection b) Venous phase 10 seconds after injection c) Anterior spinal artery course (→) d) Posterior spinal artery course (→) e) Venous phase 10 seconds after injection f) Venous phase 10 seconds after injection g) Venous phase 10 seconds after injection h) Venous phase 10 seconds after injection i) Venous phase 10 seconds after injection j) Venous phase 10 seconds after injection k) Venous phase 10 seconds after injection l) Venous phase 10 seconds after injection m) Venous phase 10 seconds after injection n) Venous phase 10 seconds after injection o) Venous phase 10 seconds after injection p) Venous phase 10 seconds after injection q) Venous phase 10 seconds after injection r) Venous phase 10 seconds after injection s) Venous phase 10 seconds after injection t) Venous phase 10 seconds after injection u) Venous phase 10 seconds after injection v) Venous phase 10 seconds after injection w) Venous phase 10 seconds after injection x) Venous phase 10 seconds after injection y) Venous phase 10 seconds after injection z) Venous phase 10 seconds after injection

### Results

In all examinations the anterior spinal artery and arteria radiculo-medullaris magna were identified. In most cases we noted several spinal cord veins, of which some were difficult to identify precisely. A summary of the phlebograms is given below.

|   | Number<br>of cases |
|---|--------------------|
| Spinal cord veins filled including identification of vena radiculo-medullaris magna | 16                 |
| Spinal cord veins filled but vena radiculo medullaris magna not identified          | 10                 |
| Spinal cord veins filled but technically poor examinations                          | 3                  |
| Spinal cord veins not filled  | 11                 |

The most consistently identifiable vessel was the posterior spinal vein which was seen in approximately 75 percent of the examinations. It was well seen in the

paired. According to SAHS (1942) the diameter of the anterior spinal vein in the Rhesus monkey averages 0.1 mm in the dorsal region and 0.25 mm in the lumbar area. The diameter of the posterior spinal vein averages 0.25 mm in the dorsal region and 0.6 mm in the lumbar area. The difference in size is approximately 2.5 times in corresponding areas, and similar differences in the anterior and posterior veins of human spinal cords might be expected.

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Fig 3 a) Simultaneous filling of arteries and veins of the spinal cord Arteria radiculo-medullaris magna ( $\Rightarrow$ ) Anterior spinal artery ( $\rightarrow$ ) Vena radiculo-medullaris magna ( $\Rightarrow$ ) Posterior spinal vein ( $\rightarrow$ ) b) Barium injected autopsy specimen of same spinal cord A single large radicular vessel on the anterior surface corresponding to the arteria radiculo-medullaris magna in (a) c) Posterior surface of same cord Veins were not injected The posterior spinal vein and vena radiculo-medullaris magna correspond exactly with the findings in (a)

than the corresponding artery. Its more gentle sweep as it enters the spinal canal and its early bifurcation into ascending and descending branches give it a 'coat-hook' appearance (Figs 3 b—c and 4).

The anterior spinal vein was demonstrated along with smaller radicular veins on the roots of the cauda equina. These filled later than the posterior spinal vein and vena radiculo-medullaris magna.

The anterior and posterior venous systems drained independently of one another. The posterior spinal vein seemed to always drain through a vena radiculo-medullaris magna in the thoracolumbar area, while the anterior spinal vein drained more inferiorly, at the caudal end of the cord, through roots of the cauda equina.



Fig. 2 Spinal cord angiography in Rhesus monkey. a) Arterial phase 2 seconds after injection. Arteria radiculo-medullaris magna ( $\rightarrow$ ) Anterior spinal artery ( $\rightarrow$ ) b) Venous phase 2 seconds later. Posterior spinal vein ( $\rightarrow$ )

low thoracolumbar area where its diameter is greatest. It may have a slightly tortuous appearance when compared to the straighter course of the anterior spinal artery (Figs 1 and 2). However, unless the animals are rotated, both vessels may be superimposed and the films may then become extremely difficult to interpret. When these vessels were well filled, the diameter of the posterior spinal vein was 1.5 to 2 times that of the anterior spinal artery.

Other large spinal cord veins visible in the films were the vena radiculo-medullaris magna and anterior spinal vein (Figs 1, 2 and 3 a). We were able to define the location of the vena radiculo-medullaris magna in 16 cases; the distribution is given below.

| Root      | Number<br>of cases |
|-----------|--------------------|
| Left Th12 | 3                  |
| Left L1   | 2                  |
| Right L1  | 2                  |
| Right L2  | 6                  |
| Left L2   | 2                  |
| Left L3   | 1                  |

The location of the vena radiculo-medullaris magna varied less than that of the arteria radiculo-medullaris magna. The vein was found to lie between Th12 and L2 in 15 of 16 examinations.

The configuration of the vena radiculo-medullaris magna is slightly different



Fig 3 a) Simultaneous filling of arteries and veins of the spinal cord Arteria radiculo-medullaris magna ( $\rightarrow$ ) Anterior spinal artery ( $\leftrightarrow$ ) Vena radiculo-medullaris magna ( $\rightarrow$ ) Posterior spinal vein ( $\rightarrow$ ) b) Barium injected autopsy specimen of same spinal cord A single large radicular vessel on the anterior surface corresponding to the arteria radiculo-medullaris magna in (a) c) Posterior surface of same cord Veins were not injected The posterior spinal vein and vena radiculo-medullaris magna correspond exactly with the findings in (a)

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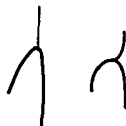


Fig 1 Schematic diagrams of 'hairpin' configuration of arteria radiculo medullaris magna (left) and 'coat hook' configuration of vena radiculo medullaris magna (right)

### Discussion

During the course of our investigations, we initially felt that the posterolateral spinal arteries and posterior radiculo-medullary arteries were being seen in the late phase. However, there is an apparent discrepancy between the small size of these vessels and the quite large vessels demonstrated on the angiograms. Furthermore, autopsy did not confirm our initial impressions, making it quite clear that we were dealing with veins. Of particular interest was the occasional large vessel that we interpreted to be a large posterior radiculo-medullary artery (Fig 3 a). After reviewing the autopsy specimens, it was clear that this vessel was the vena radiculo-medullaris magna (Fig 3 b and c).

SCHIECHTER & ZINGESSER (1966) demonstrated the spinal cord arteries in humans during direct vertebral angiography. In 4 of 100 examinations, they claimed to identify both the anterior and posterior spinal arteries in the lateral view. We have also seen similar vessels filled during the late phase in vertebral angiography. Similar vessels on the anterior and posterior aspects of the cord can also be seen during experimental angiography in the monkey (Fig 5). On the basis of our new knowledge about spinal cord veins, we feel that it is more likely that the posterior spinal vein was demonstrated rather than the posterior spinal artery. Apparently, this vein will fill, while the anterior spinal artery still remains filled.

Much of the difficulty distinguishing spinal cord arteries from veins is due to the lapse of less than two seconds from maximal venous filling. A selective intercostal injection from a possible but unverified case of hemangioblastoma of the spinal cord is given in Fig 6. The films were exposed at 0.5 second intervals. The enlarged anterior spinal vein filled maximally two seconds after the anterior spinal artery. Both the artery and the vein were filled during much of the sequence, a finding that can lead to faulty interpretation. Spinal cord arteries and veins were often seen filled at the same time during experimental angiography as well (Figs 3 a and 7).



Fig 5 Lateral view. Anterior spinal artery and posterior spinal vein (arrows) outlining the entire cervical spinal cord. The posterior spinal vein can be traced over posterior surface of the medulla.



Fig 6 Selective angiography via intercostal artery in case of possible spinal cord hemangioblastoma. Ap view of thoraco-lumbar spine. Sequential films at 0.5 second intervals. Filling of enlarged anterior spinal artery (left arrow) quickly followed by filling of enlarged posterior spinal vein (right arrow).



In many of our experimental investigations the spinal veins filled one second after the filling of the anterior spinal artery. The rapid spinal cord circulation could have been due to the pharmacologic action of levophed. Besides elevating the blood pressure, levophed diverts the contrast medium into the spinal cord circulation by constricting peripheral and splanchnic vessels. This vasoconstriction is also responsible for delayed emptying of the aorta, intercostal and lumbar arteries, which causes prolonged filling of the anterior spinal artery. Although this mechanism explains why arteries and veins were seen filled by contrast medium at the same time, it does not satisfactorily explain the appearance of venous filling only one second after arterial filling.

In order to further clarify the role of levophed in shortening the spinal cord circulation time, we performed angiography using a different technique. A balloon inflated to 250 mm Hg (Di Chiro et coll 1970) was used to externally compress the abdominal aorta during angiography. Even without the use of levophed, we still obtained a rapid spinal cord circulation time. To further confirm this finding, we recorded the circulation time.

Films were taken of dye (coomassie blue) circulating in the surgically exposed spinal cord vessels. We roughly calculated a circulation time for dye to flow from the anterior spinal artery to the anterior spinal vein of 1 to 1.5 seconds. Perhaps, the best explanation for rapid venous filling in the spinal cord is the rather small capillary bed separating the arterial and venous systems.

Although the simultaneous presence of arteries and veins can pose problems, certain diagnostic benefits can also be derived. For example, in the lateral projection of the mixed arterial and venous phase (Fig 7), the anterior and posterior limits of the spinal cord are clearly outlined down to the conus.

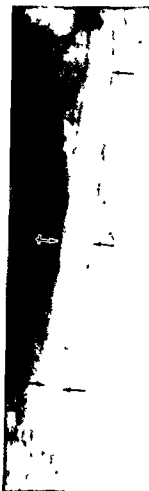


Fig 7 Lateral view. Both anterior spinal artery (→) and posterior spinal vein (←) filled. The vessels converge at the conus.

## SUMMARY

The venous phase in spinal cord angiography was demonstrated by experimental techniques using Rhesus monkeys. The radiographic anatomy of the posterior spinal vein, vena



## EFFECTS OF WATER SOLUBLE CONTRAST MEDIA ON THE MICROCIRCULATION IN PERIPHERAL NERVES

Registration of flow by microphotoelectric plethysmography

by

S. E. SORENSSEN and M. ASANO

The haemodynamic effects of water soluble contrast media intravascularly administered have been the subject of comprehensive investigations (FISCHER & ECKSTEIN 1961, BROWN et coll 1965, FODA et coll 1965, TINDALI et coll 1965, KLOSTER et coll 1967, LFSFN & MUNKNER 1968, FISCHER et coll 1968, CORNELL 1968). The intraarterial injection of such contrast media has produced a characteristic increase in cardiac output and a decrease in blood pressure, interpreted as indications of reduced peripheral resistance with resulting increased peripheral blood flow. LINDGREN & CORNELI (1958) and LINDGREN et coll (1967, 1968) confirmed these findings, by injecting contrast media into the femoral artery of the cat by the method of photoelectric drop-recording described by LINDGREN & UYNAS (1954) and LINDGREN (1958) they demonstrated an increased blood flow volume in this vessel. HILAL (1966) observed the same circulatory effect of contrast media by determining the regional blood flow with an electromagnetic flowmeter. Information concerning the changes in blood flow in, e.g. an extremity

after the intravascular exhibition of various contrast media, was obtained by both methods. The techniques of recording regional blood flow described do not however permit an analysis of the possible changes in distribution of blood in microvascular nutritive compartments in the extremities caused by different contrast media, nor is it possible to make a detailed evaluation of the extent to which tissues are influenced by the circulatory changes. It was therefore considered important to carry out a vital microscopic analysis of peripheral microcirculatory events after the intraarterial injection of contrast media, a method that would enable qualitative and quantitative analysis of their effects to be made. A tissue to be examined by vital microscopic techniques, must satisfy two requirements (1) be readily accessible and able to be exposed with minimal injury in a living animal and (2) be so thin that it can preferably be transilluminated. The tibial nerve of the rabbit and the perineural tissue in the same region appear to satisfy these requirements (LUNDBORG & BRÄNEMARK 1968, LUNDBORG 1970).

The side effects have always been considered mainly to be due to the hypertonicity of the contrast media generally used. In this investigation the significance of hypertonicity of the solutions injected has been analyzed by the injection of a sodium chloride solution with an osmolality almost equal to that of Isopaque Cerebral and Urografin 60 %.

### Material and Methods

*Animals* Rabbits of both sexes about 1 year old and weighing about 1.5 kg were anesthetized with urethane (0.75 to 1.0 g/kg) and heparin (10 mg/kg) as anticoagulant intravenously, tracheotomy was performed to facilitate respiration. The room temperature was maintained at 22° C.

*Nerve preparation* The tibial nerve was carefully exposed by the technique of LUNDBORG & BRÄNEMARK and LUNDBORG and irrigated with Tyrode's solution at room temperature to prevent dehydration. The section of the nerve illuminated and under observation was protected by a piece of very thin glass.

*Microscope for observation* A modified binocular Leitz intravital microscope was used for analysing the microcirculatory condition and behaviour. At the same time the blood flow changes in the microcirculatory area were recorded by the method of microphotoelectric plethysmography described by ASANO et coll (1964, 1965, 1970). This technique has for the first time made it possible for the dynamic behaviour of the microvascular events in a selected area to be recorded continuously and quantitatively. One eye piece was used for recording the total microphotoelectric plethysmogram. The field displayed was transmitted to a monitor via a closed circuit TV system (TV 601-1 Fernseh GmbH, Germany).

A simultaneous analysis of changes in blood flow volume and blood flow velocity can be made by segmental microphotoelectric plethysmography with this TV image and by recording it on videotape. The knee joint was immobilized by a specially designed stand to eliminate movements of the vascular image due to pulsations, respiration, body movement etc.

*Equipment for total and segmental microphotoelectric plethysmography.* Microphotoelectric plethysmography (MPPG) has been described in detail elsewhere by ASANO et coll. and will only just be mentioned. The equipment for total MPPG is composed of a CdS photoconductive cell (MKY-7STA, Mori Rikagaku, Japan), a balance controlling bridge (own construction by ASANO et coll.), and a multichannel recorder (ABEM, 119 5E 5K-24, Sweden). The dynamic behaviour of the microcirculation is recorded on the total MPPG via one ocular of the microscope. A simultaneous direct vital microscopy analysis can be performed through the other eye-piece. The equipment for segmental MPPG consists of three CdS cells, three balance controlling bridges, a large camera obscura which has a focussing screen and the above mentioned recorder. The microvascular image on the TV monitor is projected onto the focussing screen. The three CdS cells for segmental MPPG are placed on the projected images of individual vessels. The dynamic behaviour, changes in the blood flow volume and velocity, characteristic patterns of the blood column in single vessels etc. are recorded on the segmental MPPG simultaneously with direct visual observation of the TV image.

Spikes recorded by passing a standard glass plate through the light beam under the microscope stage (for the total MPPG) and in front of the camera lens (for the segmental MPPG) can be regulated in amplitude and adjusted to the same level so that the sensitivity can be calibrated. Accordingly, in the actual MPPGs increases in calibre of the vessels as well as in the blood flow in the microcirculation are recorded as an ascending wave, decreases being recorded as a descending wave, an interruption of the blood column in a single vessel, for example a plasma space or blocking of blood flow, is recorded as a downward spike or a dip in the tracing on the segmental MPPG. The records are obtained both continuously and quantitatively. The fluctuations of the base line, the indentations, the vertical spikes and the interruptions in MPPGs are objectively recorded as sensitive registrations of changes in behaviour in the microcirculation. Alterations in the base line of both the total and segmental MPPG were used for evaluation of changes in the blood flow volume and the indentations and spikes of the segmental MPPG were employed for measuring fluctuations in the blood flow rate.

*Determination of blood flow rate.* The principle for determining the blood

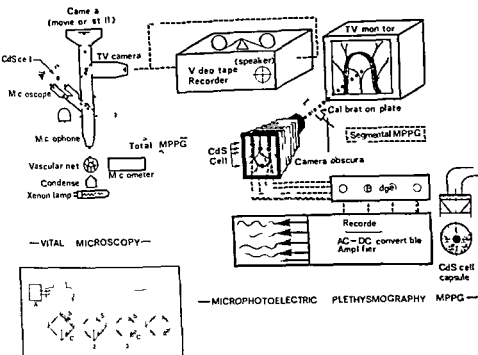


Fig 1 Diagrammatic representation of experimental set up

flow rate has been described in detail elsewhere (ASANO et coll) and again will only be mentioned. The flow rate is obtained in the segmental MPPG by recording the time during which an erythrocyte or a plasma space passes two fixed points in the vessel and measuring the distance between these points. The timing is carried out on tracings of the paralleled segmental MPPGs conducted from the fixed points in the image. The time interval between corresponding spikes or oscillations means the time during which an erythrocyte or a plasma space passes from the proximally localized photocell to the distal one on the same vessel. The actual distance in the vessel between the measuring points is determined by means of a micrometer. The flow rate may therefore be determined precisely, continuously and objectively as distance/time.

*Procedure for microphotelectric plethysmography* A record of the total MPPG is made from the whole image of a microcirculatory area from all arterioles, capillaries and venules in the intra- or extraneural system in the actual area. Registrations in this investigation were made at fairly high magnification ( $\times 230$ ) only from the intraneural system. The segmental MPPG registrations

Table

*Chemical characteristics of the contrast media used (based on data from Nyegaard & Co Oslo)*

|                    | Iodine concentration<br>(mg I/ml) | Osmotic pressure<br>converted to NaCl<br>concentration<br>(g/100 ml 20° C) | Viscosity<br>(cp 20° C) |
|--------------------|-----------------------------------|--|-------------------------|
| Physiologic saline | —                                 | 0.90   | 1.01*                   |
| Hypertonic saline  | —                                 | 4.60**   | 1.07*                   |
| Isopaque Cerebral  | 280                               | 4.51   | 7.0                     |
| Isopaque Coronary  | 370                               | 6.50   | 17.5                    |
| Isopaque 260       | 260                               | 4.24   | 3.4                     |
| Urografin 60 %     | 290                               | 4.68   | 7.3                     |
| Urografin 76 %     | 370                               | 6.27   | 19.2                    |

\* Based on Landolt Bornstein *Physikalisch-chemische Tabellen* p. 138 Berlin 1929

\*\* Concentration of sodium chloride solution used in the experiments

were performed from arterioles, capillaries and venules at low magnification ( $\times 80$ ). Recordings for measuring the blood flow rate were made through the videotape recording system at a magnification of  $\times 100$ . By this procedure a simultaneous analysis of blood flow volume and blood flow velocity was possible by utilization of the image reproducibility with the aid of videotape registration. The paper speed on the recorder was 5 cm/min during the analysis of blood flow volume and 100 cm/min for the determination of the blood flow rate. Diagrammatic representation of the experimental set-up is given in Fig. 1.

**Drugs** The contrast media and sodium chloride solutions in this investigation are given in the Table. All were injected by hand into the abdominal aorta through a polythene catheter placed in the left renal artery with the tip 0.5 cm from the origin of the renal artery from the aorta. The amount injected was 1.0 ml/kg and the temperature of the solutions about 22° C, the injection time varied between 0.5 and 1.0 sec. An interval of at least 10 min elapsed between each injection.

**Blood pressure** The carotid pressure was recorded continuously with an electro-manometer (Pressure Transducer 267 A and 161 Recorder, Sanborn, USA) during the whole experiment.

## Results

**Systemic blood pressure** A momentary rise in blood pressure ranging from 30 to 40 mm Hg ('blood pressure' is here used to indicate mean blood pressure unless reference to systolic or diastolic is specifically made) occurred on injection

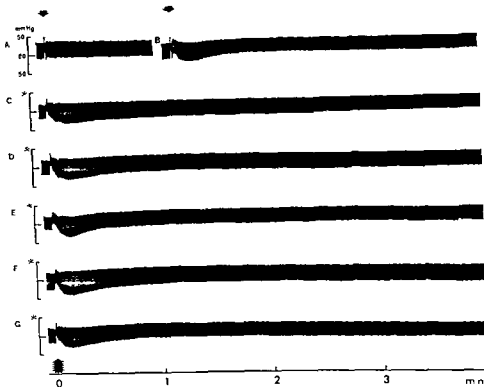


Fig 2 Responses of systemic blood pressure to intraaortic injection of contrast media. A) Physiologic saline B) Hypertonic saline C) Isopaque Cerebral D) Urografin 60 E) Isopaque Coronar F) Urografin 76 G) Isopaque 260. RI = rest. \* = increase in blood pressure; • = decrease in blood pressure; ◊ = no change in blood pressure.

presumably due to a hydrostatic effect on the abdominal aorta. The different solutions tested also produced various other blood pressure effects. After inter-

duration of 3 to 5 sec then again occurred, no recognizable pressure change followed (Fig 2 A)



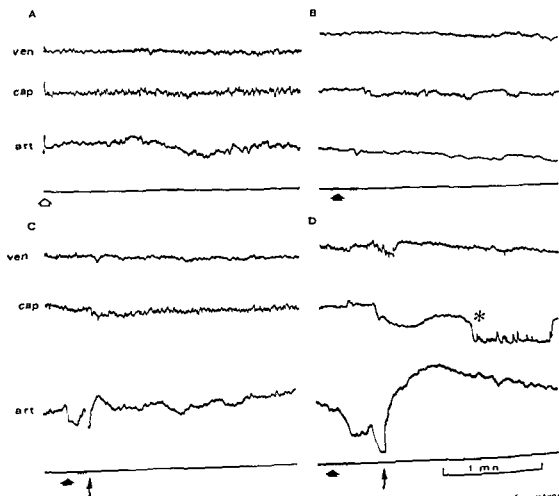


FIG 3 Response of extraneural microvascular system to intraaortic administration of contrast medium A) Control level before injection B) Physiologic saline C) Hypertonic saline D) Isopaque Cerebral Open and thin black arrow indicate calibration spike and passage of solution respectively (also employed in subsequent figures) A clear biphasic response to the contrast medium composed of a first slight depressing and a second phase panel D is evident The second phase is characterized by arteriolo-venular hyperaemia and by passing of the capillary Blocking of capillary flow at\*

creased by about 5 mm during 15 to 30 sec, and a third phase with the pressure increasing to a maximum of about 5 mm above the initial pressure during 1 to 3 min (Fig 2 B)

Isopaque Cerebral and Urografin 60 % caused the same triphasic response The change in blood pressure and the duration of the second and third phases were different from those caused by the hypertonic saline, whereas those in the first phase were almost the same In the second phase a decrease of about 10 mm for 20 to 60 sec was noted In the third phase an increase of about 5 mm for 2 to 5 min was registered Moreover, the change in diastolic pressure in the second

phase was more marked than after administration of hypertonic sodium chloride solutions whereas the systolic pressure in both the second and third phases were changed to a minor degree. Isopaque Coronar and Urografin 76 % caused the same triphasic response as the preceding two contrast media. The change in blood pressure response and duration of the second and third phases after injection of these high-concentration media were different from those of Isopaque Cerebral and Urografin 60 %, whereas those in the first phase were almost the same, in the second phase a decrease of 10 to 15 mm in 20 to 30 sec and in the third phase an increase of 5 to 10 mm in 6 min, respectively, occurred. Ispaque 260 caused the same triphasic response as the above mentioned contrast media and change in blood pressure and the duration of the response placed this contrast medium between Isopaque Cerebral and Isopaque Coronar in effect. Regarding the responses of blood pressure a comparison between the Isopaque group and the Urografin group indicated that the Urografin contrast media were more active.

The first phase blood pressure response could not always be isolated from the hydrostatic effect of the solutions injected. The more viscous the solution the more difficult the demarcation between the responses appeared to be.

**Heart rate** Physiologic saline caused no obvious change in the heart rate. Hypertonic saline and all the contrast media produced a bradycardial effect coinciding with the latter half of the first and the second phase of the blood pressure response. The administration of Isopaque Coronar and Urografin 76 % sometimes led to transient arrhythmia in addition to the regularly occurring bradycardia.

**Respiration** Physiologic saline caused a slight hyperventilation for a short time after the injection. The contrast media produced a similar effect in all the first, second and third phase of the blood pressure response. The hyperventilatory response was greater the higher the concentration of the contrast media administered.

### *Microcirculation in the nerve*

**Blood flow in the extraneural system** (nutrient vessels and outermost part of epineural vessels). During direct microscopy and in the segmental MPPG registrations from a single microcirculatory unit (i.e. a series of vascular segments composed of a single arteriole-capillary-venule channel) spontaneous rhythmic fluctuations in the microcirculation of the nerve were observed as previously demonstrated in the microcirculation of cutaneous tissue (Asano et coll 1965, 1968, 1970). The basic component was the so-called  $\alpha$  wave with a frequency

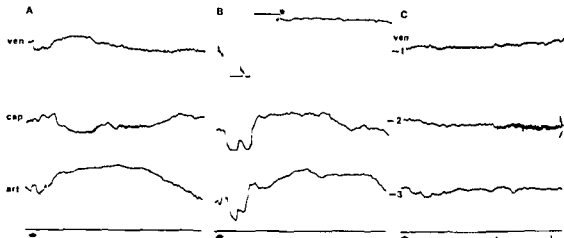


Fig 4 Different response patterns of extraneural microvascular system to intraaortic administration of contrast medium depending on vascular condition A) Arteriole, true capillary and venule within a single microcirculatory unit B) Arteriole throughfare channel of capillary (arteriole venular shunt in its function) and venule within a single unit C) Three venules from different units joining a single vein at the same level A) Typical response pattern consisting of a first depressing and a second paradoxical phase B) Hyperaemic response registered even in capillary flow C) The change in blood flow varies in each venule depending on the communication to capillaries and other venules

of 1 to 4 cycles/min,  $\beta$  waves and  $\gamma$  waves were also registered. The spontaneous rhythmic fluctuations, however, in microcirculation of the nerve were considered negligible in demonstrating the effects of the administered drugs as the spontaneous fluctuations were small. Passage of the solutions in all the extraneural vessels of the nerve occurred 2 to 15 sec after their injection. The passage time (this term means the time during which the solution injected inside the microvascular lumen passes the single CdS cell) in the microcirculatory area amounted to 3 to 15 sec. The passage was distinctly recorded in the MPPG (as in Figs 3 D, 5, 6, 8). After the injection of physiologic saline the passage could sometimes not be demonstrated even though it was clearly observed in the same area after the injection of contrast media. The latent period was longer the more viscous the solution, as was the passage time. If the drugs tested are listed according to these data the following succession would be obtained: physiologic saline < hypertonic saline < Isopaque 260 < Isopaque Cerebral < Urografin 60 % < Isopaque Coronar < Urografin 76 %.

The considerable variations in the duration of the latent period and passage time of the solutions were probably due to differences in the condition of the selected microcirculatory areas even in the same animal.

Physiologic saline caused no noteworthy changes in the microcirculation (Fig 3 B), although hypertonic sodium chloride solution produced biphasic changes

(Fig 3 C) The first phase with a decrease in the arteriolar flow for 5 to 10 sec, including the passage time, started just after the injection and this effect was observed as a slowing down of the blood flow velocity, often accompanied by a decrease in the haematocrit (This was not so clearly demonstrated in capillaries and venules) A second phase was then noticed just after passage of the solution with a duration of about 10 sec in which a slight increase in the blood flow and diameter of the arteriole but scarcely any in the venule could be demonstrated. On the contrary a little decrease or no change was evident in the capillary blood flow (Fig 3 C)

Isopaque Cerebral caused the same biphasic pattern of response, i.e. the first phase of depression of the microcirculation (in the following 'the first phase' of the microcirculatory change includes both the initial period with decreased flow and the passage time) for 20 to 30 sec just after the injection, the second phase consisted of a marked arteriolar and a slight venular increase in flow and diameter of the vessels with a duration of 1 to 5 min immediately following the passage of contrast medium. Sometimes no change occurred in the venular flow in the second phase. The contrast medium in the true capillary caused however an obvious decrease in the flow with a duration of 1 to 5 min, which coincided with the second phase of the arteriolar and venular responses, or more often took place just after the passage of the contrast medium through the capillary at the end of the first phase (Figs 3 D, 5 A, 5 C, 7 A, 9). This second decrease in the capillary flow sometimes resulted in a complete block in the blood flow as marked in Figs 3 D and 6 A. These findings indicate a shunting of blood flow from arteriole to venule via communicating anastomoses (arteriolo-venular shunt), Fig 4 A depicts a characteristic biphasic response in a microcirculatory unit where there was no such shunt. Fig 4 B represents another characteristic response in the arteriolar and venular flow patterns in a unit in which the capillary was considered to constitute an anastomosis between an arteriole and venule according to its function, an increase in the blood flow occurred even in the capillary. Fig 4 C presents three flow patterns in venules joining the same vein. The vascular response is different in the three venules, in venule — 1 consisting of an increased, — 2 decreased, and — 3 a transient decreased flow.

Urografin 60 % caused exactly the same type of response as Ispaque Cerebral in the microcirculation. The magnitude of the response to Urografin however, tended to be higher. Ispaque Coronar and Urografin 76 % also produced the same pattern of reaction as the preceding two contrast media but these high-concentrated media were more potent and caused greater changes of longer duration. This was often more than 5 min and moreover these compounds appeared to induce effects and to be active in animals in which the earlier mentioned contrast media, including Ispaque 260, hardly led to any disturbances.

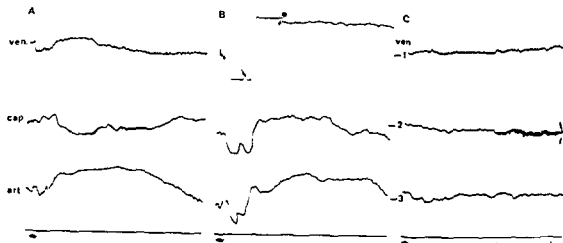


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in the microcirculation at all (Fig 5) Isopaque 260 was associated with the same type of response as the other contrast media with its intensity tending to place it between Isopaque Cerebral and Isopaque Coronar

No intravascular rheologic changes in blood cells, such as aggregation of erythrocytes or the adhesion of leucocytes to the endothelium or thrombus formation, could be demonstrated after the injection of the hypertonic sodium chloride solutions or contrast media

*Blood flow in the intraneural system* (epineural vessels other than those of the outermost part and the perineural and fascicular vessels) The intraneural microvasculature is characterized by numerous divergent anastomoses between the microvessels The intrafascicular vascular plexus consists mainly of capillaries and venules (LUNDBORG 1970), it was consequently difficult to find a separate microvascular unit to the microscopy field without complex communications with other parts of the microvascular system The total MPPG was therefore considered suitable for registration of the effects of the drugs on the regional microcirculatory flow The spontaneous rhythmic fluctuations in the intraneural vascular system proved to be negligible in the present investigation

Even in the intraneural vascular system, passage of the solutions injected was registered by the MPPG in the same way as observed in the extraneural system, the latent period and the duration of passage time tended however to be longer, i.e. about 3 to 20 and 5 to 15 sec, respectively Fig 6 depicts the passage of a contrast medium (Isopaque Cerebral) in an extra- and intraneural system in adjacent regions Passage of the contrast medium injected could not always be registered as evident in the extraneural microvascular area. The fact that it was not always possible to demonstrate the passage of the solution administered, the length of the latent period (i.e. the period from injection to the appearance of the medium injected in the microvascular area) and the duration of the passage, varied according to differences in microvascular conditions in the areas selected Flow rates slowed down in the latent period and a decrease in the haematocrit was often recorded Latent periods and passage times were longer the more viscous the solutions If listed according to the same principle as on p 409 physiologic saline < hypertonic saline < Isopaque Cerebral < Urografin 60 % < Isopaque Coronar < Urografin 76 %

Physiologic saline caused no change in the intraneural microcirculation reg

Fig 5 Comparison of responses in the same extraneural microvascular system to contrast media A) Isopaque Cerebral B) Urografin 60 % C) Isopaque 260 D) Isopaque Coronar Passages of media The high concentration medium Isopaque Coronar caused a + + + + +

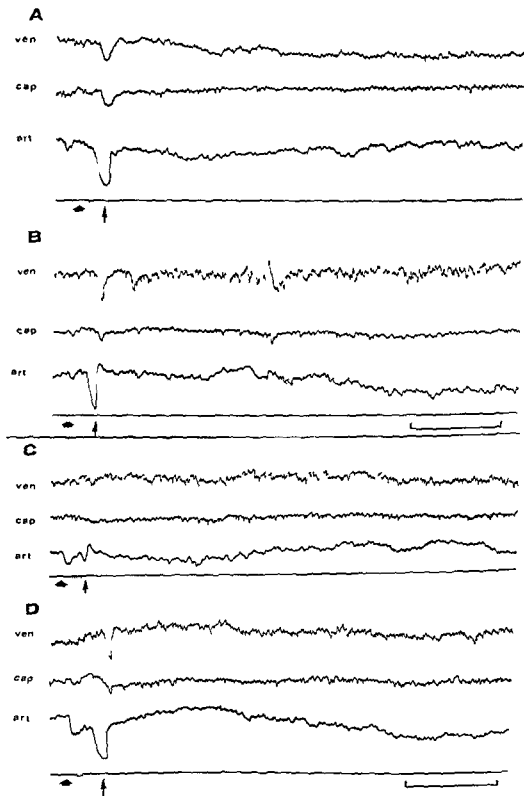


Fig 5 (For legend see opposite page)

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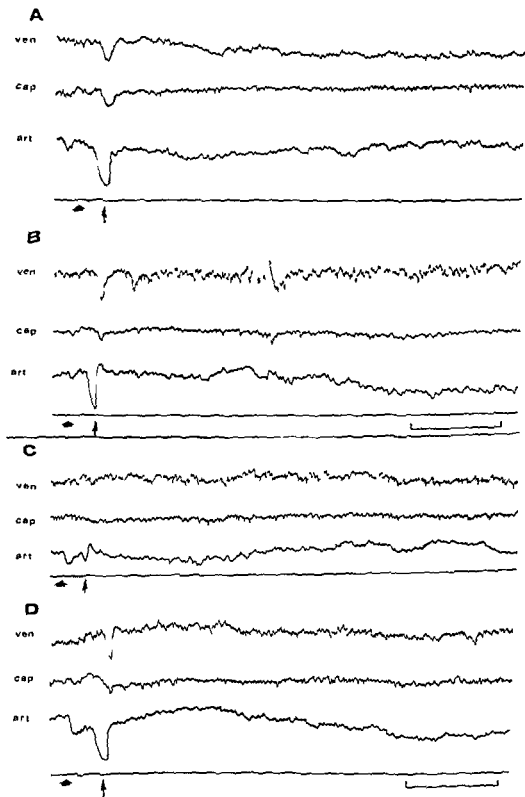


Fig 5 (For legend see opposite page)

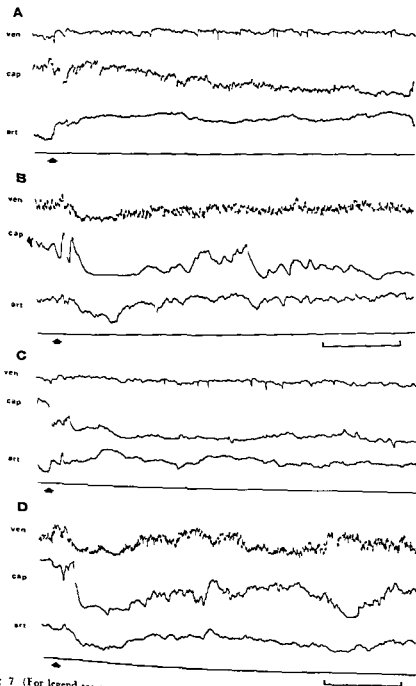
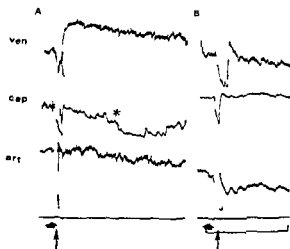


Fig 7 (For legend see opposite page)

Fig 6 Comparison of responses in extra and intraneural microvascular systems in the same animal to intra-aortic administration of contrast medium A) Extra- and B) intraneural system Isopaque Cerebral (\* indicates blocking of capillary flow) Typical biphasic response in extraneural system Another type of biphasic response, composed of a first slight depressing and a second ischemic phase, is however registered in the intraneural system Passage of medium is evident even in the intraneural system



istrable by direct microscopy or in the MPPGs Hypertonic saline led to a biphasic response consisting of a first phase with slight slowing down of the blood flow for 2 to 10 sec just after the injection and then a second low flow phase with slight decrease in the blood flow volume and rate with a duration of 1 to 2 min in all arterioles, capillaries and venules

Isopaque Cerebral produced the same biphasic pattern of microcirculatory response as the hypertonic saline but the second phase was more striking The arteriolar and venular flow responses in this area were reverse to the reaction in the extraneural system as earlier described, whereas the response in the true capillaries was in the same direction as in the extraneural system (Fig 7 A, 7 B) The duration of the response in the intraneural microcirculation corresponded to those in the extraneural in general, that is 20 to 30 sec for the first phase and 1 to 5 min for the second phase, respectively

Urografin 60 % initiated the same response pattern as Isopaque Cerebral The intensity of the reaction tended to be greater and the duration longer after the administration of the former Isopaque Coronar and Urografin 76 % caused the same type of responses, but these high-concentration media were more potent as also demonstrated in the extraneural microvascular system Isopaque 260 produced the same response pattern as the other contrast media and the reaction

Fig 7 Comparison of responses in the extra and intraneural micro vascular system in the same animal to intraaortic administration of Isopaque Cerebral and Isopaque 260 A) Isopaque Cerebral in extraneural system B) Isopaque Cerebral in intraneural system C) Isopaque 260 in extraneural system, D) Isopaque 260 in intraneural system After injection of both media paradoxical responses in the second phase in the extraneural system and marked ischemic responses in the intraneural system were observed Isopaque 260 tends to cause a greater reaction in the extraneural system together

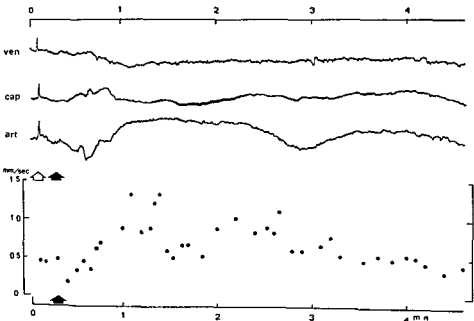


Fig 9 Comparison of change in blood flow volume and rate in the same arteriole to the intraaortic administration of contrast medium Segmental MPPG in venule, capillary and arteriole in the same microvascular unit where flow velocity is determined concurrently in the arteriole (upper part) Contrast medium Isopaque Cerebral Same response throughout the typical biphasic reaction

## Discussion

*Blood pressure, heart rate and respiration* It has been clearly demonstrated that the contrast media investigated elicit a triphasic response in the blood pressure, consisting of a first phase with increase, a second phase with decrease and a third phase with increase in the mean blood pressure (Figs 2, 10), a bradycardial response and a hyperventilatory response

A decrease in the blood pressure has been previously recorded (HILAL, LINDGREN et coll) The triphasic response in the pressure now reported has not been previously described in detail KROVETZ et coll (1967) demonstrated a similar type of pressure change in the dog after the intra aortic injection of hypertonic solutions, including contrast media, different from those employed in this investigation, these authors did not however analyze their findings more closely

*First phase* The initial transient increase in blood pressure is considered to be due to the hydrostatic effect of the contrast medium The amount of solution does not in itself affect the blood pressure regulating centres as no pressure

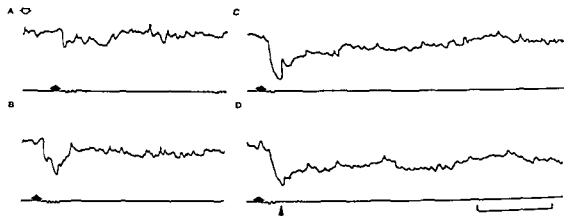


Fig. 8 Comparison of ischemic responses in the same intraneural microcirculation system to intravortic administration of Isopaque Cerebral and Urografin 60%. A) Physiologic saline B) hypertonic saline C) Isopaque Cerebral D) Urografin 60%. Passage of the solutions demonstrated. Urografin 60% tends to produce the greatest effect.

tended to be greater than with Isopaque Cerebral but less than with Isopaque Coronar.

Total blood flow in the same region in the intraneural microvascular system, as recorded by the total MPPG, was markedly reduced after the administration of all the contrast media examined and the same reaction, although less marked but clearly evident, was registered after the injection of hypertonic sodium chloride solutions. Only small changes were caused by physiologic saline. The events described are presented in Fig. 8. The reduction in blood flow in the intraneural microcirculation was greater after the administration of Urografin 60% than of Isopaque Cerebral (Fig. 8).

As in the extraneural microvascular system no intravascular rheologic changes could be demonstrated in these experiments after injection of the different solutions.

**Blood flow rate.** Direct microscopy analysis revealed that the blood flow velocity increased and decreased with an increase and decrease, respectively, in the blood flow volume. The flow velocity, however, slowed sometimes considerably with only a small decrease in the volume, especially in the first phase in both the extra- and intraneural microvascular areas. It was clear that the media produced a remarkable acceleration of the velocity in all vessels in the second phase concurrently with an increase in flow volume in the extraneural system. Arteriolar flow rate was sometimes accelerated up to about three times that of the pre-injection value. Fig. 9 represents a typical response in the extraneural microcirculation to one contrast medium (Isopaque Cerebral). Changes in flow volume and flow rate in the arteriole apparently run together.

pressure seems to be characteristic. In other words, a decrease in mean arterial pressure and an increase in pulse pressure is typical of the pressure response to the contrast media (Fig. 10). It has been demonstrated that the higher the concentration of the contrast medium, the greater the change in blood pressure.

*Third phase* This period of increase in blood pressure may be a kind of rebound phenomenon. The same effect, with reversed phase, has been observed after the administration of catecholamine in the rabbit (ASANO & NAKAMURA 1968).

*Bradycardia* reported in this investigation is the same as in previous observations and might be explained as vagal bradycardia initiated by the effect of the contrast medium on the vagus facilitating centre in the brain (LINDGREN & TORNELL 1958). The slowing down of the heart rate can hardly explain the second decreasing phase of the pressure response: the extent of the pressure decrease was not influenced to any degree by the occasional occurrence of arrhythmia in addition to the bradycardia (even if the initial part of the second decreasing phase might be caused by the bradycardia).

*Hyperventilation* The hyperventilatory response may be produced by a similar mechanism for all media since the phenomenon was demonstrated even after the injection of hypertonic sodium chloride solutions and physiologic saline. The magnitude of the response was, however, different and much less after injection of the latter. LINDGREN & TORNELL have suggested that both the decrease in blood pressure and the bradycardia after the intracarotid administration of contrast media seem to be elicited by their effect on vasomotor structures in the brain: they also felt that the major cause of the decrease in the pressure seems to be a reduction in the sympathetic vasoconstrictor tone.

All the phenomena described in this investigation—the hypotension, the bradycardia and the hyperventilation—might be explained hypothetically by postulating that the media at the same time stimulate the medial part of the vasomotor centre in which the inhibitory area is localized, the dorsal motor nucleus of the vagus nerve situated in immediate apposition to the medial part of the vasomotor centre and the respiratory centre, which is intermingled with the vasomotor centre in the reticular substance of the brain stem. Further clarification of the causes and mechanisms of the changes in blood pressure and cardiac and respiratory function is needed and requires selective pharmacologic and neurophysiologic registration methods. Additional quantitative investigations are also required to compare precisely the action and influence of different contrast media on various cardiovascular and respiratory parameters.

*Microcirculation in the epineural tissue and in the nerve* The microvascular

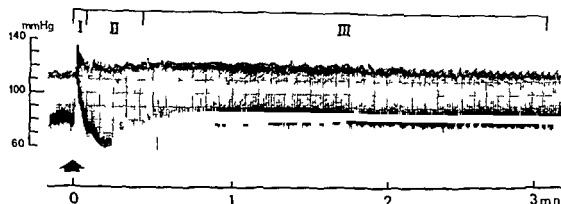


Fig 10 Typical triphasic response pattern of systemic blood pressure to intraaortic administration of contrast medium I) First phase with increase in blood pressure just after hydrostatic effect (p 410) II) Second phase with decrease in blood pressure III) Third phase with increase in blood pressure Contrast medium Isopaque Coronar

response is demonstrable after the injection of physiologic saline. The increase in pressure just after (or together with) the hydrostatic effect occurs after the injection of all solutions. The pressure response pattern is principally the same after the administration of normal saline and high concentration contrast media although the reaction is more marked after the latter, it appears to occur before the solutions reach the central nervous system. It seems reasonable in view of this to assume that the mechanism of blood pressure response now reported is the same for all the media examined including physiologic saline. In an attempt to explain the mechanism behind this first phase of the blood pressure response it should be remembered that the right kidney is placed more caudally than the left so that the vascular anatomic conditions are such that a substantial amount of the solutions injected reach the right kidney directly. It might therefore be assumed that the contrast media injected transiently obstruct the renal blood flow and increase the resistance. The greater the viscosity the more marked will be the resistance to flow and the higher the pressure response. As however, hypertonic saline causes a marked pressure response similar in pattern and time sequence to that of contrast media the hypertonicity of the solutions injected is also considered to play a major role in this phase of the blood pressure response.

*Second phase* The decrease in blood pressure after the period of increase corresponds to that reported by others (HILAL, LINDGREN et coll). Provided that general vasodilatation occurs after the passage of the contrast media in the microvascular areas distal to the injecting point this pressure response could be explained as due to the vasodilatation. However, since a marked decrease in diastolic pressure was caused only by the contrast media and this phenomenon was more striking the higher the concentration the gross fall in the diastolic

of the kidney to extract para aminohippurate suggest as an explanation that such substances produce a direct toxic effect on the tubules or intrarenal shunting. The dye diluting technique they used for studying the renal blood flow could however not demonstrate shunting with certainty because "the dye curves probably are not sensitive enough to show smaller alterations in these factors (arteriovenous shunting or alteration in intrarenal compartmental flow)". Vital microscopy, is an extremely sensitive method which reveals even very small disturbances in the microvascular area of the circulation. Analysis by microphotoelectric plethysmography has however made it possible to disclose, reproduce and record both continuously and quantitatively the pattern of even small microcirculatory events.

Registration of by passing of the capillaries has thus been attained. The hypotheses proposed by LINDGREN & TORSELL that contrast media affect the smooth muscle tissue in the vessel at the arteriolo-venular level can hardly directly explain the phenomenon of the by passing of the capillaries. If the direct effect of the medium on vascular smooth muscle cells is presumed to be vascular paralysis causing vasodilatation (GORDON et coll 1950, LINDGREN & TORSELL) it is hard to understand why a common increase does not occur in the capillary blood flow simultaneously with the arteriolo-venular shunting. A possible explanation could be that the increased flow in arteriolo-venular shunts produced by the contrast media reduces the intracapillary pressure gradient (i.e. the pressure gradient between arteriole and venule) thereby lowering the physical prerequisite for flow. The possibility of contrast media leading to damage to the endothelium of the capillaries or other disturbances in the border zone between the vessel walls as well as plasma and corpuscular elements interfering with the rheology of the blood must even be considered. It appears that

not only in the nutritive whole vascular system in the

the decrease in blood flow of the nerve that runs from the proximal level of the sciatic nerve to the distal level of the tibial nerve is accordingly not able to maintain the intraneural blood supply, this is in spite of the fact that the intraneural circulation has been demonstrated to be markedly resistant to isolation from the extraneural circulatory system (LUNDBORG & BRÄNEMARK, LUNDBORG). This decrease in blood flow in nutritive capillaries as well as in all the vessels in the intraneural system makes it reasonable to suggest that the therapeutic use of contrast media should be avoided even if it has been found to be effective in producing vasodilatation in acute spasm in arteries of the extremities (LINDGREN et coll 1959). The decrease in flow in the intraneural nutritive system could be dangerous to the tibial nerve at least, and consequently also to the tissues innervated by the nerve especially with repeated injections.



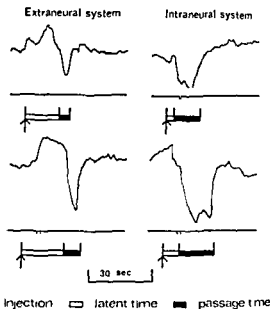


Fig 11 Comparison of passage time of Isopaque Cerebral (upper curves) and Urografin 60% (lower curves). Period from injection of contrast medium to its appearance in the microcirculation as well as the time of passage in the microvascular area longer with Urografin 60% compared to Isopaque Cerebral in both the extra- and intraneural systems. MPPGs of extra- and intraneural system have been registered from separate animals.

condition of peripheral nerve and epineural tissue is complex with numerous anastomoses between the intraneural and epineural vascular bed (LUNDBORG 1970). The abundance of arteriole-venular shunts and large venular nets are especially characteristic.

As mentioned the medium injected probably constitutes a hindrance to the blood flow peripheral to the point of injection (origin of left renal artery from the abdominal aorta). The first phase with a reduction in the blood flow in the extra- as well as the intraneural microvascular area is therefore entirely caused by the medium in the proximal part of the vasculature, thus constitutes a 'liquid plug' moving peripherally as indicated by the passage of the medium registered in the MPPG as well by direct microscopy. The higher the viscosity of the medium, the greater will be resistance to the blood flow (Fig 11). The increase in blood flow after injection of contrast media in the regional artery, as demonstrated previously by others (HILAL, LINDGREN et coll.), corresponds to the findings in this investigation in the arteriole-venular part of the extraneural microcirculation. The increased arteriolar flow after the passage of the media injected is by way of numerous anastomoses and many arteriole-venular shunts almost immediately distributed to a venular system of large capacity. This vital microscopy analysis and quantitative evaluation of the microvascular circulation has however for the first time made it possible to demonstrate that the increased flow is accompanied by a decrease in capillary flow, i.e. a shunting of blood. Other investigators have considered the possibility of media causing arteriovenous shunting (BOWER et coll 1966, DAVIDSON et coll 1965, TALNER & DAVIDSON 1968). DAVIDSON et coll and TALNER & DAVIDSON in investigating the ability

negative correlation is reasonably explained by the distance from the point of injection to the microvascular area observed. The medium is supposed to act as a 'liquid plug' constituting a transient obstruction to the blood flow distal to the point of injection and thus increasing the peripheral resistance. The circulation in the extra- and intraneural area accounts for a very small part of total blood flow and probably plays only a small role in blood pressure regulation. However, it seems reasonable to suppose that a common decrease in arteriolar or small arterial resistance in tissues that can be presumed to occur may be important for pressure regulation and that the kidney, the muscles in the lumbar area and leg, and the subcutaneous tissue may explain the main part of the second pressure change.

In addition to the direct effect of the drugs on the vessel wall causing dilatation of arterioles, a centrally controlled vascular response may also account for the hyperaemia. Further investigations are needed to explain this mechanism in tissues such as those of the kidney, muscle and skin as well as subcutaneous tissue to obtain a standardized test situation to permit exact evaluation of blood pressure response and microvascular effects of the different contrast media.

It is remarkable that vital microscopy after the injection of contrast media failed to make it possible to demonstrate intravascular erythrocyte aggregation — by American investigators called sludging — so extensively reported in the literature (READ 1959, READ & MEYER 1960, READ *et coll.* 1961, JOHNSON & KNISELY 1962, WIEDEMAN 1963, 1964, HARRINGTON & WIEDEMAN 1965, LINDGREN *et coll.* 1964, ALMEN & WIEDEMAN 1968). The discrepancy between the findings in the present report compared to those of other investigators may be attributed to the fact that the concentration of contrast media employed in several of the above mentioned investigations has been extremely high. Evaluation of some of the reports of sludge phenomena demonstrated by vital microscopy makes it obvious that the method employed in these investigations failed to permit an adequate degree of resolution and identification of corpuscular elements and intercorpuscular relations of the blood.

## Conclusions

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... could nerve and perineural tissue in the rabbit

In the first phase a reduction of the blood flow for about 20 sec was registered and in the second phase increased arteriolo-venular flow, accompanying a phenomenon of by passing of the capillaries for 1 to 5 min, was demonstrated. At the

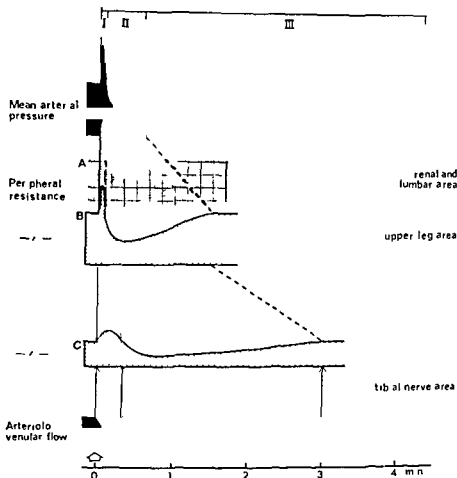


Fig 12 Schematic representation of interrelation between response in systemic blood pressure and tibial nerve microcirculation to intraaortic injection of contrast medium. The solutions are supposed to cause plugging in the vascular system distal to the injection sites thus increasing flow resistance. The first increasing phase in blood pressure may be the result of this effect of the media injected in proximal areas such as the renal, intestinal and lumbar areas as well as in the legs. The result of increased resistance to flow in proximal areas is a decrease in flow volume and rate in the microcirculation of the tibial nerve. Passage of the medium in the microcirculatory areas distal to the injection site results in a decrease in peripheral resistance with subsequent increased flow in the microcirculation followed by a decrease in the blood pressure. The indicated duration of the increase and decrease in peripheral resistance in (B) (upper leg area) is based on an illustration by LINDGREN et coll (Acta radiol (1964) Suppl No 270 p 44 Fig 3). The third increasing phase of the blood pressure change may be a kind of rebound phenomenon.

A schematic representation of the relation between the biphasic change in the extraneural arteriolo-venular flow (channel) and the triphasic change in blood pressure is presented in Fig 12. An increase (decrease) in mean arterial pressure against a decrease (increase) in extraneural arteriolo-venular flow is noted. This

## RÉSUMÉ

Les auteurs ont étudié sur le lapin la réponse de la pression sanguine à l'injection intra-arterielle de moyens de contraste tels que l'Isopaque et l'Urografin, ainsi qu'à l'injection de serum salé physiologique et de serum salé hypertonique. Ils ont pratiqué simultanément une analyse en microscopie vitale de l'effet micro-circulatoire de ces différentes solutions sur le nerf tibial du lapin. Ils ont mesuré et enregistré ces effets sur la micro-circulation par une plethysmographie micro-photoélectrique.

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- FODA M T, CASTILLO C A, CORLISS R J et coll The intravascular space —
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termination of the first phase the passage of the solution through the micro vessels was noted as a flow with low haematocrit

The contrast media and the sodium chloride solutions caused no intravascular rheologic changes in blood cells, but produced a distinct triphasic response in the blood pressure concurrently with the microcirculatory changes. Changes in the mean pressure were as follows: a first increasing phase amounting to 10 to 20 mm Hg with a duration of 3 to 5 sec, a second decreasing phase of 10 to 15 mm and 30 to 60 sec duration, and a third increasing phase of about 5 mm and 2 to 5 min duration. In the second phase, a striking decrease in the diastolic pressure was recorded especially after the administration of the high-concentration contrast media. Bradycardial and hyperventilatory responses were clearly observed, starting at the last half of the first and continuing during the second and third phases of the blood pressure changes. Implications of these findings have been discussed, especially the possible significance of the specific condition of the microcirculation in the tibial nerve and perineural tissue, the role of the intravascular 'plugging' of the medium, as well as the increased arteriolar venular flow.

### Acknowledgements

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### SUMMARY

The blood pressure response to the intraarterial injection of contrast media such as Isopaque and Urografin as well as of normal saline and hypertonic sodium chloride solutions was investigated in the rabbit. Simultaneous vital microscopy analysis of the microcirculatory effect of the various solutions was carried out on the tibial nerve of the rabbit. Evaluation and registration of the effects on the microcirculation were performed by microphotoelectric plethysmography.

### ZUSAMMENFASSUNG

An Kaninchen wurde das Verhalten des Blutdruckes nach intra arterieller Injektion von Kontrastmitteln, wie z. B. Isopaque und Urografin, als auch von Normalsalz und hypertonschen Salzlosungen studiert. Gleichzeitig wurden vitalmikroskopische Studien der Wirkung dieser Losungen auf den Tibialnerven der Tiere vorgenommen. Mit Hilfe der mikrophotoelektrischen Plethysmographie wurden Schitzungen der Einwirkung dieser Substanzen auf die Mikrozirkulation gemacht.

## ADVERSE REACTIONS DURING UROGRAPHY AND MODIFICATION BY ATROPINE

by

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Many of the more severe reactions occurred following the application of the ureteric compressors. The time the reaction commenced, its nature and its severity were recorded. It was sometimes not possible to record the blood pressure or pulse rate. The reactions are grouped into those occurring before and those after the compression was applied.

*Reactions before compression* A total of 330 cases received contrast medium only. 196 cases had 0.5 mg atropine intravenously plus the contrast medium and

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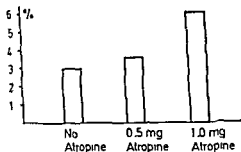


Fig 1 Incidence of reactions (all mild) before compression

were so severe that no pulse rate or blood pressure could be recorded. One patient who developed a reaction that caused the examination to be discontinued was given 0.5 mg atropine intravenously on recovery and following this the examination was successful.

*Mild reactions* These were termed mild when either the compression was not released, or if only partially released, was not associated with severe cardiovascular disturbance (i.e. either a pulse rate less than 60 or a blood pressure less than 80). The reactions were again the common ones of nausea, sweating and pallor sometimes with accompanying mild hypotension.

The onset of the reactions occurred from immediately up to 20 min after the compression was applied, with the peak at 10 min (Figs 4, 5). Atropine led to an increase in the incidence of the mild reactions, particularly in a dose of 0.5 mg where there was an increase from 3 to 6 per cent, 1 mg atropine produced 7 per cent of reactions (Fig 6). On the other hand the incidence of severe reactions fell with increasing dosage, from 6 to 3 per cent with 0.5 mg atropine and to 1 per cent with 1 mg atropine.

### Discussion

Contrast medium alone produced an incidence of 3 per cent of reactions before compression in this series. Atropine is known to give rise to palpitations and skin rashes and would be expected to contribute its own quota of untoward reactions. This was confirmed (Fig 1) by a 0.5 per cent rise in incidence when 0.5 mg atropine was used and a further rise to 6 per cent with 1 mg atropine. It is perhaps a little surprising that atropine despite its mild anti-emetic effect produced no effect on nausea.

Therapeutic doses of atropine occasionally cause an active vasodilation of cutaneous blood vessels especially of those in the blush area — atropine flush (GOODMAN & GILLMAN 1956). The mechanism is unknown. The distribution

**Table**  
*Nature of reactions before compression*

|  | Reactions |                   |          |           |              | No of patients |
|--|-----------|-------------------|----------|-----------|--------------|----------------|
|  | Nausea    | Nausea and pallor | Vomiting | Rash      | Palpitations |                |
| Contrast medium only                               | 4         | 2                 | 2        | 1 (0.3 %) |              | 330            |
|  | 2.4 %     |                   |          |           |              |                |
| 0.5 mg atropine intravenously plus contrast medium | 5 (2.5 %) |                   |          | 2 (1.0 %) |              | 196            |
| 1.0 mg atropine intravenously plus contrast medium | 4 (2.0 %) |                   |          | 6 (3.0 %) | 2 (1.0 %)    | 197            |

197 cases received 1 mg atropine intravenously before the contrast medium. The reactions were nausea, pallor, vomiting, skin rashes and palpitations. All were transient and mild and tended to occur with or soon after the injection of the contrast medium or atropine. The Table indicates that nausea and vomiting and occasional skin eruptions were attributable to the contrast medium. Atropine increased the number of rashes and in the 1 mg dosage caused palpitations. The rashes were unspecified in the 'contrast only' series and in both atropine series the blush area was more obviously involved.

No reduction in nausea was brought about by the atropine. A dose of 0.5 mg of atropine increased the incidence of reactions slightly from 3 to 3.5 per cent, with a 1 mg dose the incidence rose to 6 per cent (Fig. 1).

*Reactions beginning after compression.* Of the patients in whom compression was applied 259 received contrast medium only, 184 had 0.5 mg atropine intravenously plus contrast medium and 171 received 1.0 mg atropine plus contrast medium.

A reaction was graded as severe if it led to the complete release of the compression, or if the compression was partially released and associated with signs of cardiovascular collapse (either pulse rate less than 60/min or systolic blood pressure less than 80 mm Hg). The decision to release completely the compression was always made by a radiologist after assessment of the pulse rate and blood pressure.

Nausea, sweating and pallor were early signs of a reaction and most commonly continued to bradycardia and hypotension. The reactions in 4 patients

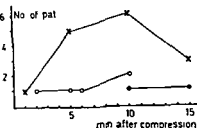


Fig 4 Time of onset of severe reactions after compression No (x), 0.5 mg (O) and 1.0 mg (●) atropine, respectively

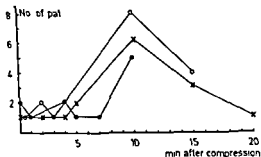


Fig 5 Time of onset of mild reactions after compression No (x), 0.5 mg (O) and 1.0 mg (●) atropine, respectively

The patients described by HOLMES (1960) who developed supine hypotension syndrome of pregnancy nearly invariably had bradycardia. BRIGDEN et coll (1950) have described a single patient developing a considerable fall in systolic blood pressure accompanied however by a nearly doubled heart rate. LEES et coll concluded that the mechanism of these circulatory events consequent on compression of the inferior vena cava may vary. The severe compression reactions in the present series, were invariably associated with bradycardia when a pulse record was obtained.

Compression reactions occurring during urography are thought by THULESIUS (personal communication) unlikely to be due to vena caval obstruction. He cited the fact that many patients undergo bilateral leg plethysmography with sudden interruption of venous return from both legs without exhibiting this syndrome, and attributed the reaction to stimulation of receptors in the viscera by the compression. However, it may be concluded that atropine has reduced the incidence of severe cardiovascular effects of compression and that this indicates that a vagal mechanism is involved on the efferent side. The vagal reflex may be triggered by the stimulation of nerve endings in the vicinity of the ureters or perhaps by obstruction of venous return. The severity of these reactions may not be widely recognized though reversal is rapid when the compression is released, the risk to the patient must be considerable. A further

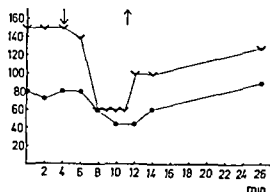


Fig 2

Fig 2 Systolic blood pressure (V) and pulse rate (●) estimated from simultaneous ECG in a patient who developed hypotension and bradycardia 7 min after compression was applied ↓ denotes compression on and ↑ compression off

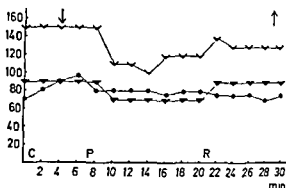


Fig 3

Fig 3 Systolic (V) and diastolic (▼) blood pressure and pulse rate (●) estimated from simultaneous ECG showing mild hypotension and bradycardia 7 min after compression was applied ↓ denotes compression on and ↑ compression off

of the rash when specified in the present material usually lay in the bluish area.

The reactions that commonly occurred after compression was applied (nausea, pallor, sweating, bradycardia and hypotension) resembled the vasovagal fainting syndrome. Many types of reflex cardiac slowing initiated through the vagus nerves were prevented by adequate amounts of atropine (GOODMAN & GILLMAN 1956), which was the rationale for its trial in prophylaxis. The compression reactions bear a strong resemblance to the reactions of the supine hypotension syndrome (HANSEN 1942). In this syndrome adoption of the supine posture in late pregnancy may cause hypotension and bradycardia—usually ascribed to obstruction of the venous return in the inferior vena cava by the pressure from the pregnant uterus (BRIGDEN *et coll* 1950). LEES *et coll* (1967) were able to demonstrate a fall in right atrial pressure and cardiac stroke volume in pregnant women near term when the supine position was adopted. This was associated with increased systemic vascular resistance, which compensated for the fall in cardiac output so that systolic blood pressure remained unaffected (6 patients). However, 2 patients developed abrupt bradycardia, with falls in systemic vascular resistance and resulting hypotension. In a further series of 6 patients the inferior vena cava was completely occluded for 25 min by external compression during caesarian section. Venous pressure below the occlusion rose abruptly from 8 to 37 mm Hg and the right atrial pressure fell from 8 to 4 mm Hg by the end of the occlusion period. There was no change in heart rate or systolic or pulse pressure in any of the 6 patients.

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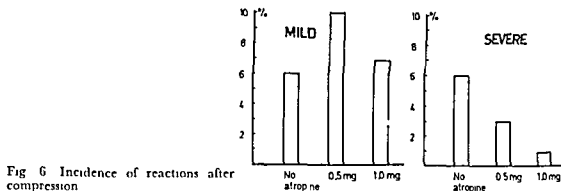


Fig 6 Incidence of reactions after compression

consideration is the low degree of excretion of the contrast medium and the poor films consequent to the hypotension (WICKBOM 1950, EDLING et coll 1954).

In conclusion the intravenous injection of 1 mg atropine in urography with compression is advocated, except when eye disease may be present.

### SUMMARY

The frequency and nature of reactions during urography and the part played by ureteric compression are discussed. Atropine reduced the incidence of severe reactions caused by compression but led to an increase in the mild reactions. Its employment is advocated to combat the former except in the presence of eye disease.

### ZUSAMMENFASSUNG

Die Häufigkeit und die Natur der Reaktionen, die sich während Urographie ereignen und die Rolle der Ureterenkompensation an diesen Erscheinungen werden besprochen. Atropin reduzierte das Vorkommen schwererer Reaktionen, die durch Kompression verursacht waren, aber führte seinerseits zu einer Vermehrung der leichten Reaktionen. Atropin wird für die Untersuchungen mit Kompression empfohlen, jedoch mit Ausnahme solcher Fälle, die an einer Augenerkrankung leiden.

### RÉSUMÉ

Les auteurs examinent la fréquence et la nature des réactions au cours de l'urographie et discutent le rôle joué par la compression urétérale. L'atropine réduit la fréquence des réactions graves causées par la compression mais augmente la fréquence des réactions bénignes. Son emploi est conseillé pour combattre les réactions graves sauf dans le cas où il existe une affection oculaire.

Table  
*Age and sex distribution*

|       | Age range in years |       |       |       |       |       |       | Total |
|-------|--------------------|-------|-------|-------|-------|-------|-------|-------|
|       | 11—20              | 21—30 | 31—40 | 41—50 | 51—60 | 61—70 | 71—80 |       |
| Men   | —                  | 1     | 1     | 3     | 2     | 2     | —     | 9     |
| Women | 1                  | 1     | 4     | 3     | 3     | —     | 2     | 14    |
| Total | 1                  | 2     | 5     | 6     | 5     | 2     | 2     | 23    |

indwelling vascular catheters, four of which were venous. They found thrombi on all of the catheters after 5 to 23 days, with no clinical signs of thrombosis.

The aim of this investigation was to study systematically by phlebography the frequency and development of thrombus formation after peripheral intravenous infusions. Phlebographic findings are related to clinical signs.

The terms 'thrombus' and 'thrombosis' are used by the present authors to denote intravascular thrombotic processes demonstrable at phlebography. 'Thrombophlebitis' is reserved for the clinical signs associated with superficial phlebitis or periphlebitis, in accordance with the general clinical use of these terms in Scandinavia.

*Method.* Phlebography was carried out according to the principles described elsewhere (BERGÅLL, to be published). The technique will be briefly described.

The limb was placed with the peripheral part (hand or foot) elevated, close to the vertical. Venous stasis was created proximal to the infusion cannula by a pressure of 70 mm Hg. Three or four films were exposed in different projections with a horizontal beam during injection of Urografin 45%, not more than 40 ml of contrast medium in all were given during the stasis. The application time before the stasis was relieved, amounted to 30 to 60 seconds. The technique is defined as centripetal descending phlebography with stasis.

For comparison, a number of examinations were performed in the same cases with an ascending technique similar to the one described for the lower limb by GREITZ (1954). The limb was placed with the peripheral part lowermost, otherwise conditions were the same as in centripetal descending phlebography. The technique is defined as centripetal ascending phlebography. Venous stasis was not used. In ascending phlebography two films were exposed in different projections during injection of a further 20 ml of contrast medium.

The patients were examined clinically at each phlebography, as well as on discharge from the hospital. Most of the patients were questioned about symptoms 1 or 2 weeks after the infusions. However, no attempt was made

## PHLEBOGRAPHIC INVESTIGATION OF INFUSION THROMBOPHLEBITIS

by

U BERGVALL and A-E EKLUND

Parenteral infusion is generally performed by means of an intravenous plastic cannula or catheter which is left in the vein until no longer required or until complications occur. Thrombophlebitis is the most frequent complication. Serious conditions caused by infection, local circulatory disturbances and accidental loss of catheter fragments are also encountered (HASTBACKA et coll 1965, JONES 1967, COLLINS et coll 1968). The figures given for the frequency of complications—almost without exception estimated clinically—vary over a wide range, depending mainly on the duration of the infusions. KVISSELGAARD & KAAIUND JENSEN (1964) pointed out that back flow of fluid along the cannula is a sign of infusion thrombophlebitis detectable before other clinical signs have appeared. They also reported a case (confirmed at autopsy) with superficial venous thrombosis but no local signs, the patient died 32 hours after the insertion of the intravenous infusion catheter. JACOBSSON et coll (1969) and JACOBSSON & SCHLOSSMAN (1969a) demonstrated the mechanism of platelet adhesion and thrombus formation on arterial and venous catheters. JACOBSSON & SCHLOSSMAN (1969b) studied systematically by angiography a small number of cases with

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Submitted for publication 12 February 1970



Fig 2 Large aggregations (→) on cannula and central thrombosis 27 hours after insertion of cannula

Glucose was always infused, usually together with fructose in a 10 to 20 % solution pH 3 to 4. Occasionally, amino acid solution, fat, blood and antibiotics were also administered. An intravenous anaesthetic, usually a short acting barbiturate, was given through the cannula in 14 instances. Dextran 70 (Macrodex 500 ml) was infused in one case. Neither heparin nor dicumarol were administered.

### Results and Discussion

The phlebographic findings were grouped into four categories (Fig 1)

*Normal findings* (3 examinations) no apparent intravascular changes. In two instances narrow segments of the cannulated vein were noted, these may be interpreted as local spasm.

*Aggregation* (7 examinations) in addition to possible spasm small, often irregular, filling defects were seen as deposits on the cannula or in the immediate vicinity, they were interpreted as platelet aggregates or early thrombus formation.

*Thrombosis* (22 examinations) floating or mural thrombi were observed, possibly in addition to spasm or aggregation.

*Occlusion* (9 examinations) not contrast filled segments of the cannulated vein, not ascribable to artefacts, appeared. Changes listed above were also observed.

Characteristic findings are demonstrated in Figs 2, 3 and 4.

Diagnosis and classification of changes have offered no difficulties. Contrast filling of the injected vein was homogeneous, and the definition of detail was good in descending phlebography with stasis. Identification of defects, particularly small ones in the contrast filled veins was facilitated mainly by exposure of the films during venous stasis, the disturbing influence of streaming effects and

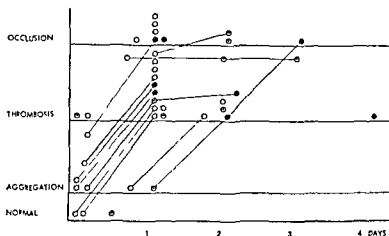


Fig 1 Phlebographic findings after infusion through 27 cannulas, repeat examinations of the same cannula are connected  
 ○ no local signs, ⊕ minor signs of thrombophlebitis, ● manifest thrombophlebitis

to cover systematically the possible occurrence of late thrombophlebitis. Two degrees of thrombophlebitis were registered: a minor degree associated with slight tenderness or a discrete infiltrate on palpation of the vein and a major degree with manifest symptoms including pain, tenderness, redness and infiltration around the vein.

**Material** This consisted of 23 patients of the age and sex given in a Table. Operation, usually abdominal surgery, had been performed within a few days of the first phlebography; in twenty patients. In one patient a floating thrombus in a calf vein was diagnosed by phlebography 7 days after cholecystectomy and 6 days after centripetal descending and ascending phlebographies through an infusion cannula in the arm. This patient recalled a similar incident a few years previously. No other patient disclosed a disposition towards thrombosis before infusion. No gestagen or oestrogen substances had been administered.

Standard disposable teflon cannulas with a metal mandrin for percutaneous puncture were used (Viggo Venflon, Stille Infart).

A total of 56 phlebographies were carried out through 27 cannulas, 41 as centripetal descending phlebographies with stasis and 15 as centripetal ascending phlebographies. One cannula was placed in the leg distally, the others in the arm between the wrist and the cubital fossa. All cannulas were shut off between the infusions for a length of time varying according to routine management principles of the department. Neither the shut off periods nor the duration of the infusions were registered.



Fig 4 Thrombosis of cannulated vein at 27 hours (upper) and occlusion from tip of cannula at 31 hours (lower)

finding other than aggregation. This may have been spasm which by local disturbance of the circulation possibly influenced the course and progress of thrombus formation (cf HASTBACKA et coll.)

The three cases with normal findings at the first phlebography later developed thrombosis or occlusion. In two, this was demonstrated at repeat phlebography but in the third case the cannula was removed because of a blockage during infusion before a repeat study could be performed.

All the seven cases with mural aggregation proved to have thrombosis or occlusion at a later examination.

Thrombosis or occlusion was noted at the first phlebography in 17 cases, in two of them within 3 to 6 hours after beginning of infusion.

Clinical signs of thrombophlebitis were observed in 14 instances. These were of minor degree in half the number of cases and of a major degree in the other half (Fig 1).

The thromboses, with few exceptions, were located at or near the tip of the cannula. The thromboses sometimes constituted small mural defects, but more often large mural or floating thrombi filled a greater part of the lumen. They had often propagated usually in a proximal direction, up to some 20 cm, and sometimes into nearby superficial veins. The deep veins were not examined by phlebography. However, no clinical signs of propagation of a thrombus to deep veins were observed. No other complications were noted.

The fate of the thrombi after withdrawal of the cannulas was not studied. It is not possible to assess the extent to which the thrombi progress into

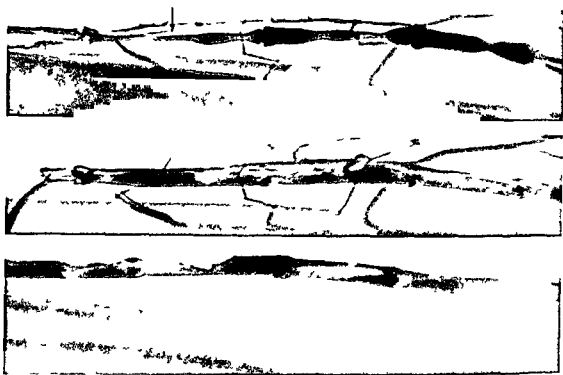


Fig 3 Narrowing of cannulated vein (arrow) at 6 hours (top) thrombosis same cannula at 27 hours (middle), and no collaterals filled with same cannula at 54 hours (bottom)

blurring being thus reduced. A sharp interphase often occurred between a contrast-filled segment and blood containing no contrast medium behind effective valves in a proximal segment. The appearance is characteristic and not likely to be mistaken for a thrombus.

These findings were compared with the concomitant ascending phlebography appearances in 15 instances: one of isolated spasm, the others of thromboses or occlusions. It appears that descending phlebography with stasis yielded more information in 12 instances, less in one, and a similar amount in another. In a final instance both methods possessed advantages, although differing in detail, the differences were generally small, and of no consequence for the diagnosis. However, a clearer conception of the distribution of the thrombotic changes was often obtained by descending phlebography with stasis. It should be noted that this method is suitable for examination of a restricted venous region but not adequate for a complete examination of the limb with presently applied levels of stasis and the amounts of contrast medium used.

Segmental narrowing of the vein around or proximal to the cannula was observed in approximately a fifth of the descending phlebographies, with no

Thrombosis or occlusion seemed to be the inevitable result of peripheral intravenous infusion with routine methods and occurred earlier than was indicated by clinical signs

Clinical signs of thrombophlebitis were recorded in 14 of the 27 instances half of a minor and half of a major degree Thrombophlebitis, clinically diagnosed, is not a reliable sign, in terms of integrity or patency, of the state of the vein receiving the infusion Phlebographic methods are necessary for such investigations as well as for determining possible means of prophylaxis

## SUMMARY

The value of phlebography in complications of peripheral intravenous infusions was investigated by means of 27 infusion cannulas in 23 cases Thrombosis or occlusion of the vein receiving the infusion always developed although with clinical signs of thrombophlebitis in only half the number of cases

## ZUSAMMENFASSUNG

Der Wert von Phlebographie bei Komplikationen nach peripherer intravenöser Infusion wurde mittels 27 Infusionskanüle in 23 Fällen studiert Obwohl klinische Zeichen einer Thrombophlebitis nur in der Hälfte der Fälle vorhanden waren zeigte die Phlebographie immer Thrombose oder Okklusion der betreffenden Vene

## RÉSUMÉ

Les auteurs ont étudié l'intérêt de la phlebographie dans le diagnostic de complications des perfusions intra veineuses périphériques en utilisant 27 trocarts de perfusion chez 23 malades Dans tous les cas il y avait une thrombose ou une obstruction de la veine perfusée cependant il n'y avait de signe de thrombophlébite que chez la moitié des malades

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segmental occlusions, or whether they regress. In this material, initial occlusion occurred in 6 cases and progress of aggregation or thrombus into occlusion in 3 cases. There were on the other hand 2 cases of thrombosis with clinical signs of thrombophlebitis in which there was no evidence of progress into occlusion at repeat examinations after 1 and 2 days. Another case, first examined after more than 4 days, had small mural thrombi as well as clinical thrombophlebitis but no occlusion.

BECKER et coll (personal communication) have demonstrated by phlebography that floating thrombi in muscle veins and deep veins of the leg may disappear spontaneously without leaving residual changes. BERGVAL & HJELMSTEDT (1968) stated that recanalisation after thrombosis occlusion of the peripheral deep veins of the leg was an unusual feature. An occluded superficial vein is not likely to offer better prospects of recanalisation. Clinical experience suggests that most of these occlusions are liable to remain permanent.

No conclusions are warranted as to the possible influence of infused contrast medium on the course of thrombosis. No observations were made that confirmed the existence of such an influence. Nor can the effect of other factors, thought to provoke thrombophlebitis, be analysed on the basis of this material.

It is of practical importance that seven out of the nine cases examined within the first 6 hours after the infusion was started had phlebographic evidence of thrombosis or prethrombotic changes, although in only one case were there clinical signs of thrombophlebitis. This indicates that the reasons for limiting intravenous infusions to 8 hours in one and the same vessel, as has been suggested (cf JONES), are invalid. The time to remove an infusion cannula should be determined from clinical complications, such as back flow, thrombophlebitis and infection.

Occlusion of peripheral veins after infusion is an important practical problem in cases requiring long term or repeated parenteral therapy. Prophylactic measures generally accepted are lacking. JACOBSSON (1969) has demonstrated the value of dextran 70 as a means of prophylaxis against thromboembolic complications of arterial catheterisation. Our results imply that systematic phlebographic studies are necessary for the investigation of possible measures to reduce the incidence of thrombosis and occlusion in peripheral intravenous infusion.

### Conclusions

Complications of peripheral intravenous infusion were investigated in 23 patients with 27 disposable teflon cannulas by phlebography with a special technique. Thrombosis or occlusion of the cannulated vein always occurred.

Thrombosis was found as early as 3 hours after insertion of the cannula.

## EXPERIMENTAL ROENTGEN EXAMINATION OF THE VESTIBULAR AQUEDUCT

by

S BRUNNER and CHR BRAHE PEDERSEN

Hydrops of the endolymphatic system was given as a cause of Meniere's disease by HALLPIKE & CAIRNS (1938). Interest has recently been focussed on the endolymphatic sac since the successful operation upon it by HOUSE (1964). A special tomographic examination is proposed in this communication to demonstrate the conditions in and around the endolymphatic duct.

*Anatomy.* The endolymphatic system includes the cochlear duct, the utricle, the saccule and the semicircular canals, these are connected with the endolymphatic duct which continues into the endolymphatic sac (Fig 1). The latter is situated on the posterior aspect of the petrous part of the temporal bone while the endolymphatic duct and sac lie in the vestibular aqueduct. The aqueduct is the osseous canal that passes from the vestibulum to the posterior aspect of the petrous pyramid and starts just medial to the opening of the common crus. It is first directed upwards and backwards, and then swings downwards and backwards to appear on the posterior surface of the petrous part of the temporal bone 1 cm lateral to the internal auditory meatus (Fig 2). The aqueduct is funnel shaped with the opening usually 2 to 6 mm in diameter but occasionally

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Fig 2 External aperture of the vestibular aqueduct ( $\rightarrow$ ) in relation to internal auditory meatus ( $\leftrightarrow$ )



a



b

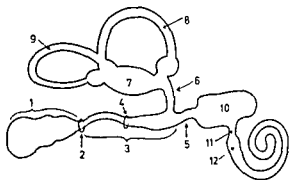
Fig 3 Tomograms of a specimen a) With and b) without copper thread in the vestibular aqueduct (arrows)

bone and describing an arch forwards and upwards, turns downwards and forwards to terminate in the vestibulum just medial to the common crus formed by the superior and posterior semicircular canals. The canal is depicted in about the same position as the external thread. The canal is filled with a Polythene thread. The specimen is examined with a Polythene thread. The correct position of the posterior surface of the petrous part of the temporal bone is controlled on a TV monitor. The central rays are focussed on the external auditory meatus. Cuts are taken up to about 2.5 to 3.5 cm below the level of the mastoid process and about 1 to 1.5 cm distal, a distance of 1 mm must be maintained between the cuts.

A tomogram typical of the semicircular canals of a normal subject is reproduced in Fig 4. The superior semicircular canal lies at right angles to the longitudinal axis of the petrous part of the temporal bone, the lateral and posterior semicircular canals present a star-like appearance.

An investigation has been commenced in which patients suffering from Meniere's disease are compared with normal controls. One of the patients has

Fig 1 The membranous labyrinth. Endolymphatic sac (1), external aperture of vestibular aqueduct (2), endolymphatic duct (3), internal aperture of vestibular aqueduct (4), saccular duct (5), utricular duct (6), utricle (7), superior semicircular duct (8), posterior semicircular duct (9), saccule (10), reuniting duct (11), cochlear duct (12).



about 10 mm in width, the opening is inclined obliquely downwards. The distal segment of the aqueduct has the appearance of a triangled space with the apex proximal to the sac. Not infrequently the fossa of the internal jugular vein is situated deeply with nothing but a thin plate of bone separating it from the endolymphatic sac. This is a typical form of the vestibular aqueduct although many variations are encountered. The most important variation is a low position of the aperture — a condition that may suggest that the sac is missing, with the aperture open at the junction between the posterior and inferior surfaces of the petrous pyramid, (ANSON 1969), the diameter of the vestibular aqueduct is not more than a few millimetres.

**Physiology.** The endolymph is produced in the stria vascularis in the periphery of the cochlear duct. DOHLMANN (1964) stated that the endolymph arises in the plana semilunata around the vestibular sensory cells. Furthermore it has been demonstrated that the endolymph flows from the cochlea and the vestibular apparatus through the endolymphatic duct to the endolymphatic sac where resorption takes place. As a supplement to this flow, radial circulation may occur inside the cochlea and the labyrinth.

The chemical characteristics of the endolymph are similar to those of the intracellular fluid but unlike those of the perilymph, the nature of which is similar to the extracellular fluid.

**Methods and investigations.** Tomographic examinations were performed on isolated temporal bones in which it had been possible to introduce a thin copper thread through the aqueduct from the posterior aspect of the petrous part to the vestibulum. These phantoms were examined in different projections, the best representation of the aqueduct was obtained in a projection in which the posterior surface of the petrous part of the temporal bone lay at a right angle to the sagittal plane. The aqueduct containing a fine copper thread is shown in Fig 3 a. It starts on the posterior surface of the petrous part of the temporal

The etiology of the hydrops has been much discussed in the literature. It is considered that it is often caused by decreased resorption, especially in the sac, in other instances it may be produced by an obliteration of the duct when the sacs are missing.

The result of operation on the sac either by its simple decompression or by hunting or incision has not been convincing, but a number of patients have become free from attacks of vertigo (HOUSE 1969, PORTMANN 1969).

It must be of practical interest to determine the anatomy of the endolymphatic sac before planning the operation. Thin section tomography of the vestibular aqueduct will render this possible. SHAMBAUGH (1969) has proved that obliteration is not rare, in some operation materials of Meniere's disease he reported that obliteration of the vestibular aqueduct occurred in about 10 per cent. VALVASSORI (1969) stated that in patients with Meniere's disease he had observed sclerosis and signs of osseous obliteration of the aqueduct.

This investigation of the vestibular aqueduct appears to be useful as a supplement to the diagnosis of Meniere's disease — a condition in which the signs are few. The result of further tomographic examinations of the aqueduct now being undertaken in patients with the disease and controls may indicate the true value of the method.

## SUMMARY

A new radiologic method of demonstrating the vestibular aqueduct is described. A future investigation in patients with Meniere's disease and in normal subjects will be necessary before a final assessment of its usefulness as a supplement to the diagnosis of this disease can be made. The work to date, however, seems to indicate that the aqueduct is sometimes obliterated in this disease.

## ZUSAMMENFASSUNG

Eine neue röntgenologische Methode zur Darstellung des Aquadukts des Vestibulums wird beschrieben. Bevor ein endgültiges Urteil über die Anwendbarkeit dieser Methode

## RÉSUMÉ

L'auteur décrit une nouvelle méthode radiologique pour mettre en évidence l'aqueduc du vestibule. Pour porter un jugement définitif sur cette méthode, il sera nécessaire d'examiner des malades atteints de la maladie de Ménière et des sujets témoins. À l'heure actuelle cependant ce travail semble indiquer que l'aqueduc est parfois obstrué dans cette maladie.

Fig. 4 Tomogram of a normal subject in the modified lateral projection of the vestibular aqueduct. Superior semicircular canal ( $\rightarrow$ ), lateral semicircular canal ( $\leftrightarrow$ ), vestibular aqueduct ( $\leftarrow$ )



a



b

Fig. 5 Meniere's disease. a) Tomogram of the normal right side in the modified lateral projection of the aqueduct ( $\rightarrow$ ) b) Tomogram of the left ear. Obliteration of the aqueduct ( $\rightarrow$ )

been a 43-year old male suffering from left-sided Meniere's disease with tinnitus, loss of hearing and attacks of vertigo. Tomography of the temporal bones revealed a completely normal right vestibular aqueduct (Fig. 5 a), while on the left side the aqueduct could not be demonstrated (Fig. 5 b).

### Discussion

Since PORTMANN (1927) proposed operation on the endolymphatic sac to decrease the endolymphatic pressure several approaches have been described. HOUSE (1964) modified these with a shunt from the sac to the arachnoidal space in Meniere's disease to facilitate the removal of endolymphatic fluid from the sac.

## BRONCHO PULMONARY VASCULAR MALFORMATION SYNDROME CAUSING LEFT HEART FAILURE DURING INFANCY

by

W. MORTENSSON and N.-R. LUNDSTROM

Malformations of the lungs are often associated with anomalies of arterial blood supply and venous drainage. The combinations of the anomalies may vary at random. However, when a special combination recurs frequently, the changes are probably due to the same interference in the embryologic organisation. An example of this is a broncho-pulmonary vascular malformation syndrome consisting of the following components: (1) Anomalous development of the right bronchial system which often is a mirror image of the left system. Bronchiectatic changes may or may not be present. (2) Hypoplasia of the right lung of varying degrees and, probably in consequence of this, hypoplasia of the right hemithorax and dextroposition of the heart. The lower part of the right lung is surrounded by thick, pleural adhesions. (3) Agenesis, or more commonly, hypoplasia of the right main branch of the pulmonary artery, which also ramifies in an anomalous way. (4) One or several arteries arise from the abdominal aorta to supply the right lung or part of it, these in relation to the lung parenchyma correspond to the pulmonary artery. (5) Total or partial

From the Roentgendagnostic Department (Director Prof. Oile Olsson) and the Pediatric Clinics (Director Prof. Bertil Lundquist), University Hospital, Lund, Sweden. Submitted for publication 26 November 1970.



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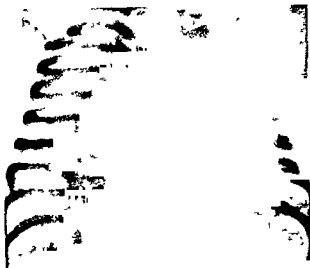


Fig 1 Case 1 The dextroposed heart fills most of the hypoplastic right hemithorax. The left lung vessels are widened. Small faintly visible curved veins run to the right cardiophrenic angle.

### Case reports

*Case 1* Girl, born after uncomplicated pregnancy. A systolic murmur was heard on the first day of life. Congestive heart failure with tachycardia, tachypnoea, intercostal retractions and enlargement of the liver, were evident at 9 days. The cardiac signs included a short mid systolic murmur (grade 2--3/6) over the entire precordial region, loudest over the left third intercostal space. ECG: Enlargement of the right atrium and hypertrophy of the right ventricle.

Röntgen examination of the chest (Fig 1). Hyperinflation of the lungs. The heart was dextropositioned and the right atrium and ventricle were enlarged. The left pulmonary vessels were widened, the right could not be evaluated. Two faintly discernible vessels curved down on the right side to the cardiophrenic angle. Heart catheterization indicated increased pressure in the right atrium (11 mm Hg), and a high oxygen level in the upper part of the inferior vena cava. The pressure in the right ventricle could not be determined due to arrhythmia. Angiocardiography (Fig 2). Enlargement of the right ventricle. The pulmonary artery and its left branch were widened. No right branch of the pulmonary artery was evident. The left lung veins emptied into the left atrium. Arteries arose, probably as one trunk and later branching from the abdominal aorta to the right lung at the level of Th12 and a few wide veins draining the lung coursed down to the inferior vena cava. The width of the aorta just before the branching of the anomalous artery to the right lung was 9 mm, while distally it was 5 mm wide.

pulmonary venous drainage of the right lung through one or several anomalous veins to the infradiaphragmatic part of the inferior vena cava. This malformation is usually called 'the scimitar syndrome' due to the curved course of this vein or veins resembling a Turkish sword, or scimitar. This figurative and indeterminate term is accepted in the medical literature and is therefore retained.

The different components of the malformation syndrome may be more or less marked. Other co-existing heart malformations, such as atrial or ventricular septal defects or patent ductus arteriosus, have sometimes been reported. The cause of the malformation syndrome is unknown. A survey of the embryologic background is given by FERENCZ (1961), only one report of a family history has appeared (NEILL *et coll* 1960). About 150 cases have been reported, mainly of adults without symptoms. Some, however, have had repeated respiratory infections, but cardiovascular symptoms were rare. The diagnosis has been made at roentgen examination of the chest, when hypoplasia of the right lung, dextroposition of the heart and a characteristic anomalous vein have been discovered.

The syndrome has rarely been diagnosed in infants, but in the few cases known, cardiopulmonary signs have been present. PARK (1912) described this malformation syndrome which he observed at autopsy of a girl aged 2 1/2 months who had fallen ill two weeks earlier with 'right-sided pneumonia'. HALASZ *et coll* (1956) reported 3 cases that during the first days of life had periods of coughing and cyanosis, and later recurrent respiratory tract infections. One of these patients, who had a ventricular septal defect as well, developed pulmonary hypertension at 4 years of age. NEILL *et coll* (1960) described a girl who at eight months of age had recurrent respiratory tract infections and later developed pulmonary hypertension. In addition to this she had a small patent ductus arteriosus, she died at 2 1/2 years after right-sided pulmectomy. SANGER *et coll* (1963), JUE *et coll* (1966) and MASSUMI *et coll* (1967) gave accounts of children who at 1 to 17 months of age had repeated respiratory tract infections, coughing and dyspnoea.

The roentgen findings of hypoplasia of the right lung and of the heart more or less occupying the right hemithorax have been wrongly interpreted as pneumonia, atelectasis or lung cysts, and as a result correct therapy has been delayed. Four of the above mentioned 8 cases described in the literature were diagnosed at roentgen examination but only when the children had reached 2 1/2 to 4 years of age. The diagnosis in 3 cases was made during operation, the children being operated upon for probable atelectasis or cysts.

The authors during recent years have investigated two infants, one aged 2 weeks and the other 9 months, with the syndrome. The clinical manifestations diverged from those described earlier.



Fig 3 As in fig 2 b but after subtraction to demonstrate the anomalous artery to greater advantage

left second and third intercostal spaces ECG Right axis deviation Atrial enlargement and hypertrophy of the right ventricle

Roentgen examination of the heart and lungs (Fig 4) Hyperinflation of the lungs dextroposition of the heart and enlargement of the right side of the heart Characteristic right anomalous veins Heart catheterization disclosed a high oxygen concentration in the inferior vena cava The relation between the pulmonary and the systemic flow was 3.5:1 with a similar mean pressure in the right and left atria (4 mm Hg) The systolic pressure was high (62 mm Hg) in the right ventricle but low in the left ventricle (72 mm Hg) The oxygen level in the left atrium and ventricle was normal Angiocardiography (Fig 5) The right ventricle and the main pulmonary artery and its main branches were enlarged The left intrapulmonary arteries were wide and tortuous The morphology of the right pulmonary artery was atypical as was its ramification The left pulmonary veins drained into the left atrium on the right side the pulmonary veins converged into one trunk which drained into the upper part of the inferior vena cava medial to which several small veins were directed towards the diaphragm An artery 5 mm wide, the intrapulmonary course of which could not be determined branched off to the right lung at the level of Th12 Before the branching of this anomalous artery to the right lung the width of the abdominal aorta was 8 mm while distally it was 4 mm Angiocardiography of the left atrium demonstrated a left-to-right shunt through an atrial septal defect Normal angiocardiography of the left ventricle

Anticongestive therapy was given but as its effect was only moderate operation was performed This revealed that the right lung consisted of two lobes the upper lobe was supplied by the pulmonary artery while the lower lobe was fed by both this artery and the anomalous artery from the abdominal aorta The venous drainage from the entire right lung flowed into the inferior vena cava The lower part of the lung was adherent to the thoracic wall

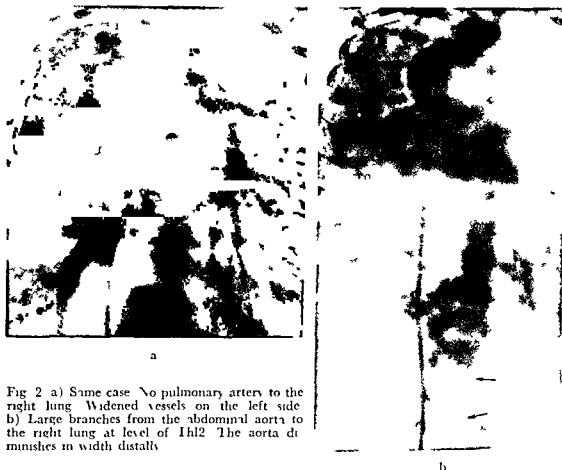


Fig 2 a) Same case. No pulmonary artery to the right lung. Widened vessels on the left side. b) Large branches from the abdominal aorta to the right lung at level of Th12. The aorta diminishes in width distally.

Since the heart failure could not successfully be treated, operation was considered necessary. The roentgen diagnosis was confirmed and it was evident that all the veins from the right lung emptied into the inferior vena cava and that most of the lung was adherent to the thoracic wall. Pulmectomy was performed. The patient had some respiratory tract infections during the following 6 months but on the whole she was symptom free and developed normally. The ECG no longer indicated signs of enlargement of the right atrium or hypertrophy of the right ventricle. Repeated roentgen examinations demonstrated that the heart volume decreased as did the width of the pulmonary vessels. While the patient was being treated at another hospital for a minor upper respiratory tract infection one year after the operation she died because of aspiration. Autopsy revealed no other malformation than those mentioned. There were no changes in the walls of the vessels in the left lung nor in the right lung removed at operation. There is no information on the bronchial system on the right side.

**Case 2** Girl born after uncomplicated pregnancy thrived well during the first months of life. From 7 1/2 months of age she began to lose weight and at nine months suddenly developed heart failure with tachycardia, tachypnoea, intercostal retractions and hepatic enlargement. Auscultation of the heart revealed a short ejection murmur loudest over the

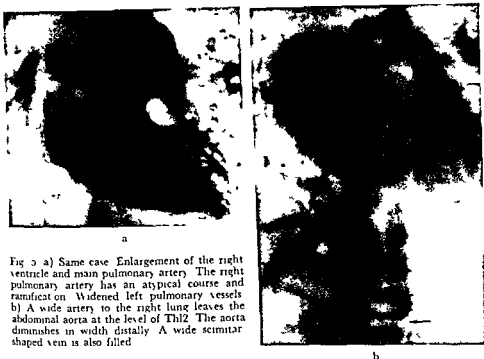


Fig 3 a) Same case Enlargement of the right ventricle and main pulmonary artery. The right pulmonary artery has an atypical course and ramification. Widened left pulmonary vessels. b) A wide artery to the right lung leaves the abdominal aorta at the level of Th12. The aorta diminishes in width distally. A wide scimitar shaped vein is also filled.

of the pulmonary veins, may be combined with some hypoplasia of the ipsilateral lung and pulmonary artery, there appears however to be no development of systemic arterial collateral vessels to the lung. The arterial blood supply to the basal parts of the lungs may frequently arise from the phrenic and intercostal arteries in different inflammatory and traumatic changes as well as in decreased pulmonary circulation. Large vessels arising directly from the abdominal aorta and running to the lungs have been observed however only in the scimitar syndrome and in cases of lung sequestrations. These vessels are to be regarded as remnants of the primitive embryologic circulation.

NEILL et coll (1960) measured a pressure gradient between the anomalous pulmonary vein and the inferior vena cava during operation but at autopsy no morphologic stenosis was evident in this region. Venous changes that could have been produced by increased venous pressure were present in the basal regions of the right lung. Neither of the present cases had hypertensive vessel changes.

It must also be borne in mind that when the opening at the tip of the catheter during pressure recording is directed against the blood stream, as occurs



Fig 4 Case 2 Dextroposition of the heart and some hypoplasia of the right hemithorax Scimitar shaped vein basally on the right side

The anomalous vessels were ligated and the lower lobe resected. The patient died however, the day following operation. Autopsy disclosed no changes in the walls of the arteries or veins. The remaining upper right lobe was small.

### Discussion

MASSUMI *et coll* (1967) maintained that in the so called 'scimitar syndrome' the only congenital malformation is the anomalous connection between a stenosed pulmonary vein and the inferior vena cava. Hypoplasia of the right lung and its pulmonary artery therefore results as a physiologic consequence. These authors suggested that a collateral circulation to the right lung is induced and systemic vessels invade the lung. Their hypothesis was based on one case in which, on recording the pressure during withdrawal of a catheter from the anomalous pulmonary vein to the inferior vena cava, a drop of 4 mm Hg was registered. No opinion was offered on the concomitant anomalies of the bronchi and the right pulmonary artery which might even have been aplastic. The literature and the experience of the present writers suggest that congenital causes of obstruction to the pulmonary venous return, such as stenosis or atresia

and the inferior vena cava is of slight or no importance

When hypoplasia of the right lung and dextroposition of the heart, irrespective of the degree, are evident at roentgen examination the possibility of their combination with vascular anomalies must be borne in mind. The curved veins going down to the cardiophrenic angle may with care be defined. The present 2 cases demonstrate that even in infancy the diagnosis may be indicated by findings at roentgen examination of the chest. These may also consist in wide pulmonary vessels to the left lung and hyperinflation of the lungs due to reduced compliance from pulmonary overcirculation.

Heart catheterisation and cardioangiography must be performed to exclude or investigate other co existing cardiovascular malformations and pulmonary hypertension. Angiocardiography will demonstrate the morphologic condition of the right main branch of the pulmonary artery. The amount of contrast medium passing to the right lung is usually sufficient to outline the anomalous and normal pulmonary veins and later the arteries from the abdominal aorta to the right lung may be evident. It may however be necessary to perform aortography to demonstrate these arteries and, with absence of or hypoplasia of the right pulmonary artery, even to demonstrate the pulmonary veins. Selective angiography has been advocated by BOIJSEN & KOZUKA (1969) in similar cases. Not only from a diagnostic but from a therapeutic point of view as well, it is important to demonstrate the systemic arteries to the right lung. After piercing the diaphragm these are embedded in pleural adhesions and difficult to observe, and if unwittingly cut heavy haemorrhage may occur.

Operation is indicated during infancy and childhood if heart failure that cannot be controlled by medical treatment exists or if the risk of the development of pulmonary hypertension is possible. For practical reasons pulmectomy must usually be the operation of choice.

## SUMMARY

The symptomatology of a broncho pulmonary vascular malformation syndrome with rare clinical manifestations is described. The diagnosis of this condition may be indicated during the first few days of life by roentgen examination with cardiac catheterisation and angiography to determine the morphologic and haemodynamic states.

## ZUSAMMENFASSUNG

Bronchopulmonales  
beschrieben. Eine  
Herzkatheterisierung  
hamodynamischen

linischen Symptomen wird  
tels Röntgenuntersuchung  
Morphologie als auch die



when the catheter is placed in the anomalous pulmonary vein, a higher pressure is recorded than when the reverse positioning occurs, such as when the catheter lies in the inferior vena cava after insertion from a femoral vein.

It has been postulated that the hemodynamic conditions in the scimitar syndrome are similar to those prevailing in atrial septal defects or when the pulmonary veins empty into the right atrium, the malformation thus results in increased loading on the right ventricle only (TAUSSIG 1960, SANGER et coll 1963, GASUL et coll 1966). The supposition regarding the increased loading due to the volume of blood carried to the right lung by the pulmonary artery and drained by the anomalous pulmonary vein holds true. A variable blood volume is however brought to the right lung by arteries from the abdominal aorta. This blood volume also represents a loading on the left ventricle and in this respect the circulatory conditions are on a par with those prevailing in left to right shunts. The flow from the aorta to the right lung has not been determined but both the width of the anomalous artery and the decrease in width of the abdominal aorta distal to this artery have indicated that the blood volume shunted is large. This explains the early onset of left heart failure. Some of the cases described in the literature (HALASZ et coll 1956, JUE et coll 1966) had signs that could have arisen from transitory left heart failure in the neonatal period.

The pressure in the right ventricle and the changes in the ECG in the older infant suggest that pulmonary hypertension existed. A case of pulmonary hypertension has been described by NEILL et coll and SANGER et coll. These authors supposed that when the increased blood flow through the lungs is concentrated in varying degrees to the left side, the risk of the development of kinetic pulmonary hypertension is increased. This hypothesis is based upon the finding that hypertensive arterial vessel changes were observed solely or mainly in the left lungs in the 2 cases now reported. This condition was also described by FERENCZ (1961) in a case with congenital absence of the right pulmonary artery, the right lung being supplied by an artery arising from the right subclavian artery, a similar case was described by BAHNER et coll (1964). The hypothesis is further supported by the fact that the pressure in the lungs at rest in congenital absence of one pulmonary artery is increased in 20 per cent of the cases, while it is increased considerably more often when simultaneous intra- or extracardial left-to-right shunting occurs.

Experiments in animals indicate that kinetic conditioned pulmonary hypertension is developed more easily in young than in older animals (RUDOLPH et coll 1961).

These findings suggest that pulmonary hypertension that may develop in the scimitar syndrome is kinetically dependent and that the pressure in the anomalous systemic arteries or the eventual pressure gradient between the pulmonary veins

## DYSCHONDROSTEOSIS

by

K KOZIOŁSKI and C ZYCHOWICZ

Dyschondrosteosis, an uncommon disease, is characterized by mesomelic shortening (of the tibiae, and fibulae, radii and ulnae) and a Madelung type of wrist deformity.

The clinical and radiographic features of the condition are consistent. It was recognized as a separate entity by LERI & WEIL (1929). Cases of dyschondrosteosis had probably been annotated previously as Madelung's deformity and, as the bone shortening was unrecognized, only sporadic cases were reported, not until the papers by CANTAGREL (1951) and KAPLAN et coll (1951), was the hereditary nature of the disease recognized. According to MOREL-PESCAROLO 1964, 27 cases of dyschondrosteosis were published up to 1963, most of them in females.

The purpose of this paper is to indicate the familial nature of dyschondrosteosis with an autosomal, dominant type of inheritance. Two of the affected members of the family reviewed are males (For further information on the disease the reader is referred to the papers of LERI et coll 1931, MAROTEAUX & LAMY 1959 and LANGER 1965).

*Genealogy.* At the time of investigation the first and second generations of the affected family were known to be diseased and information about them was

## RÉSUMÉ

Description des symptômes d'une malformation vasculaire bronchopulmonaire avec des manifestations cliniques rares. L'examen radiologique avec cathétérisme cardiaque et angiocardigraphie dans les premiers jours de la vie peut permettre le diagnostic de cette affection et l'étude de l'état morphologique et hémodynamique.

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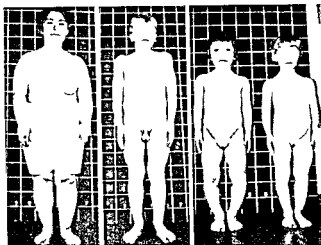


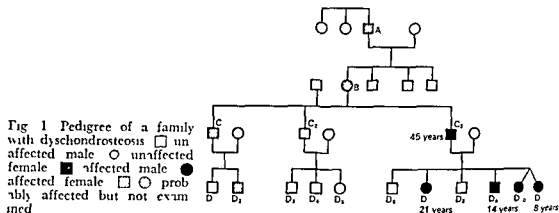
Fig 2 Photographs of patients D7 D9 D10 and D11 Mesomelic type of shortened stature although both proximal and distal segments are involved Lateral bowing of the legs No other gross deformities are visible The Madelung type of deformity much more convincing in the roentgenograms than on clinical examination

mann reaction was negative The mucopolysaccharides in the urine were not increased

*Roentgen examination* The radiographic features of dyschondrosteosis have been described by LERI & WEILL (1929), LERI et coll. (1931), CANTAGREL (1931), KAPLAN et coll. (1951), MAROTEAUX & LAMY (1959), MOREL PESCAROLO (1964), LANGER (1965)

A summary of the findings in the members of the present family is as follows. Full skeletal examinations indicated that the skull, spine, thoracic cage and pelvis were normal in each case Proximal limb bones, hands and feet presented certain atypical deformities, most marked in the older subjects. The diagnostic radiographic changes were localized to the forearm, wrists and lower legs.

*Forearms* The radius and ulna were both shortened, with a varus deformity of the former and an increase in the distal joint space between the deformed radius and the hypoplastic ulna (Fig 3) The radial interosseous ridge was well marked and the radial head small and flattened The radial head in D7 was broad and deformed with a relatively narrow neck and accentuation of the tuberosity The distal radial epiphysis was flattened, producing a wedge shaped deformity The ulna was short and thick with a varus curve of the proximal half Distally it was subluxated posteriorly to the radius and this subluxation caused a



obtained from their descendants. Both A from the first generation and his daughter B from the second generation were said to be of short stature (Fig 1). In the third generation, B has 3 sons (C1, C2 and C3), two of whom, C1 and C3, are of short stature. In the fourth generation, C1 has 2 sons (D1 and D2) one of whom, D2, is of shortened stature, C2 has 3 unaffected children. Of the 6 children of C3 4 (D7, D9, D10 and D11) are affected.

**Histories** All the affected members, C3, D7, D9, D10 and D11, attended the clinic because of shortened stature. They were otherwise healthy and had no other symptoms except for sporadic knee pain (in D9) and ankle pain (in D10).

C3 does not remember his own early history, but stated that all of his children in generation D were full term infants at birth, and subsequently had normal motor and psychologic development. For the first two years of life their rate of growth was normal, but thereafter it was noticed that they were smaller than other children of their age, and that this difference became more marked in subsequent years. They had suffered no serious illnesses.

**Physical examination** All members of the family affected with dyschondrosteosis had shortening of stature of the midsegmental (mesomelic) type. Slight deformity was also apparent in the distal part of the forearms due to subluxation of the distal end of the ulna relative to the radiocarpal bones. The wrist movements were normal. The lower ends of the tibiae and fibulae presented a varus deformity, most marked in the twins, the distance between the knees being 7 and 6 cm in D10 and D11, respectively. The head, face, chest and abdomen were normal in all patients, and the physical development according to their ages was as illustrated in Figs 1 and 2. Some measurements of the patients are given in the Table.

**Biochemical results** Routine blood and urine examinations were normal, as were the serum Ca, P, alkaline phosphatase and cholesterol levels. The Wasser-



Fig 3 Dyschondrosteosis in a woman aged 21 (D7) Wrist and forearm deformities characteristic of dyschondrosteosis Radioulnar subluxation was more convincing in this film than clinically

believe however, that its differentiation from these diseases presents any real difficulty. It is more likely that doubt may arise with hypochondroplasia and Turner's syndrome, especially if only single films of the hand or knee have been taken. Even so, neither the forearm nor knee deformities are characteristic of either of these two diseases (KOZŁOWSKI & ZYCHOWICZ 1964). A diminished carpal angle is present in both, although it is usually much more marked in dyschondrosteosis. The Madelung type of forearm deformity has been described in Turner's syndrome (Kosowicz 1962) but it is possible that these were in fact cases of dyschondrosteosis. On the contrary, cases described as examples of dyschondrosteosis with a positive Archibald's sign (a line drawn tangentially to the circumference of the heads of the fourth and fifth metacarpals runs through the distal end of the third metacarpal, in normal subjects — negative Archibald's sign — it passes distal to the head of the third metacarpal) (ARCHIBALD 1959), were probably Turner's syndrome. The Kosowicz sign (enlargement of the proximal medial tibial metaphysis) (Kosowicz 1962), may be present in both diseases. Osteoporosis is absent, and the bone age may be normal in dyschondrosteosis.

Table

*Some physical measurements of the patients with dyschondrosteosis*

| Case and age  | Height (cm) | Weight (kg) | Circumference of the head (cm) | Breadth (cm) | Distance between symphysis and sole (cm) |
|---------------|-------------|-------------|--------------------------------|--------------|--|
| C3 (45 years) | 151         | 60.5        |                                |              |  |
| D7 (21 years) | 135         | 62.1        | 53.5                           | 135          | 64                                       |
| D9 (14 years) | 137         | 13.3        | 55.0                           | 139          | 64                                       |
| D10 (8 years) | 110         | 24.6        | 51.5                           | 109          | 48                                       |
| D11 (8 years) | 109         | 22.6        | 51.5                           | 107          | 48                                       |

secondary deformity of the carpal bones, the semilunar bone being displaced proximally between the radius and ulna, and the carpal angle diminished.

*Legs* (Figs 4, 5 and 6) The tibia and fibula were short and broad with a varus deformity at the knee joint. The medial side of the proximal tibial epiphysis was flattened and there was associated enlargement and flattening of the adjacent part of the metaphysis. This deformity was sometimes so marked as to resemble an exostosis. In Case D9 a similar 'exostosis' was present on the medial aspect of the distal femoral metaphysis (Fig. 4). Some flattening and deformity of the distal tibial epiphysis was also present.

*Other deformities* The femoral and humeral shafts were slightly shortened and broadened, with some deformity of the head and anatomic neck of the humerus, with shortening of the latter. The metacarpals were also shortened (Fig. 7).

### Discussion

Dyschondrosteosis is a rare type of dwarfism and may therefore be unfamiliar to both radiologists and paediatricians. Few reports are to be found in the English literature (BERDON et coll. 1965, LANGER 1965), most publications being in the French language. The condition is seldom recognized before puberty and up to this age the dwarfism is only moderate and the Madelung type of deformity symptom free. Both the clinical and radiographic findings are however characteristic and there is little difficulty in recognizing the disease once its existence is suggested.

In the differential diagnosis, achondroplasia, multiple exostoses, the Ellis-van Creveld syndrome and both pseudo- and pseudo-pseudo-hypoparathyroidisms must be taken into account (BERDON et coll. 1965). The present authors do not



Fig 3 Dyschondrosteosis in a woman aged 21 (D7) Wrist and forearm deformities characteristic of dyschondrosteosis. Radio-ulnar subluxation was more convincing in this film than clinically.

believe however, that its differentiation from these diseases presents any real difficulty. It is more likely that doubt may arise with hypochondroplasia and Turner's syndrome, especially if only single films of the hand or knee have been taken. Even so, neither the forearm nor knee deformities are characteristic of either of these two diseases (KOZŁOWSKI & ZICHOWICZ 1964). A diminished carpal angle is present in both, although it is usually much more marked in dyschondrosteosis. The Madelung type of forearm deformity has been described in Turner's syndrome (KOSOWICZ 1962) but it is possible that these were in fact cases of dyschondrosteosis. On the contrary, cases described as examples of dyschondrosteosis with a positive Archibald's sign (a line drawn tangentially to the circumference of the heads of the fourth and fifth metacarpals runs through the distal end of the third metacarpal, in normal subjects — negative Archibald's sign — it passes distal to the head of the third metacarpal) (ARCHIBALD 1959), were probably Turner's syndrome. The Kosowicz sign (enlargement of the proximal medial tibial metaphysis) (KOSOWICZ 1962), may be present in both diseases. Osteoporosis is absent, and the bone age may be normal in dyschondrosteosis.



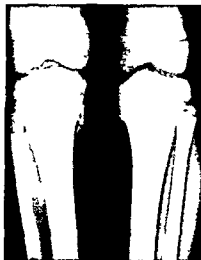


Fig 4

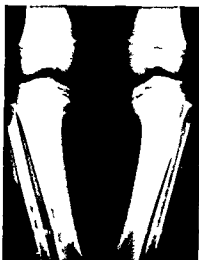


Fig 5



Fig 6

Fig 4 Dyschondrosteosis in a boy aged 14 (D9). Shortening and deformity of the leg bones and knees evident. Exostoses of the medial aspects of the femoral and tibial metaphyses are suggested.

Fig 5 Dyschondrosteosis in a twin girl aged 8 (D10). Similar changes to those in fig 4 are already visible although much less marked. The deformities of the medial aspects of the proximal tibial metaphyses are well defined.

Fig 6 Dyschondrosteosis in a twin girl aged 8 (D11). Similar changes to those in fig 5 but less marked. The constancy of the radiographic features among members of the same family is apparent.

Mesomelic dwarfism of the hypoplastic ulna fibula mandible type (LANGER 1967) may cause further confusion.

One of the clinical uncertainties about dyschondrosteosis, which should be mentioned is its relation to primary Madelung's deformity (secondary Madelung's deformity develops subsequently to infection or trauma of the distal part of the radius). A review of the literature suggests that dyschondrosteosis was probably not recognized in many cases described as primary Madelung's deformity with some shortening of the stature. ANTON *et coll.* (1938) noticed among 171 cases with Madelung deformity, 8 cases with shortened stature. PAUS (1951) observed 30 cases of Madelung's deformity in one family, many of which were of short stature. Similar observations were made by KARLSSON (1956) and MARTINE-DUBOUSQUET (1958).

According to MOREL-PESCAROLO (1964), Madelung's deformity may exist as a localized lesion associated with normal stature, as is also the experience of the present authors. On the other hand LANGER (1965) believes that Madelung's disease and dyschondrosteosis are the same condition. It seems that only further detailed observations of cases of Madelung's deformity will decide whether the



Fig 7 Dyschondrosteosis in a man aged 45 (C3) Shortening of the tubular bones particularly the metacarpals Deformity of radial and ulnar articular surfaces with diminished carpal angle

two diseases are homogeneous or heterogeneous with different expressions of the same gene. For this reason it is suggested that all patients with Madelung's deformity should have their height recorded and their lower limbs examined. The preponderance of women among the patients with dyschondrosteosis should also be proved, as an autosomal dominant type of inheritance points to equal distribution among both sexes.

The observations of the family now reported are in accord with MOREL-PESCAROLO (1964), who suggested some variability in the severity of affection within each family. It seems that among the present patients women were more severely affected than men.

### Acknowledgement

The authors wish to thank C. J. Hodson for his helpful criticism.

### SUMMARY

Five cases of dyschondrosteosis caused by a dominant gene in two generations of one family are described. The histories suggest that four other members of the family were affected. In all instances the radiographic findings corresponded with the classic descriptions of appearances that were already evident in the two youngest patients, 8 year old twin girls.

## ZUSAMMENFASSUNG

Beschreibung von fünf Fällen von Dyschondro Osteose, die durch ein dominantes Gen in zwei Generationen einer einzigen Familie auftritt. Nachforschungen in die Familiengenealogie machten es wahrscheinlich, dass vier andere Familienmitglieder an derselben Erkrankung litten. In allen Fällen entsprachen die Röntgenercheinungen dem klassischen Bild, das sich auch in den zwei jüngsten Patienten, Mädchen von acht Jahren, fand.

## RÉSUMÉ

Les auteurs décrivent cinq cas de dyschondrostéose causés par un gène dominant dans deux générations d'une famille. L'interrogatoire fait penser que quatre autres membres de cette famille étaient atteints. Dans tous les cas les signes radiographiques ont correspondu aux descriptions classiques des aspects qui étaient déjà évidents chez les deux plus jeunes malades, deux jumelles âgées de 8 ans.

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## ROENTGEN APPEARANCE OF PROSTATIC CHANNELS IN INFANCY AND CHILDHOOD

by

GEORG THEANDER

The numerous ducts of the prostate gland are provided with minute orificial flaps of tissue that normally prevent the inflow of urine from the urethra. Nevertheless, at urethrocystography contrast medium is sometimes seen to enter a variety of channels or cavities in the prostate. This abnormal finding may indicate the existence of truly abnormal lumina or merely the orificial insufficiency of ducts that ordinarily open into the urethra.

Whereas certain anomalous lumina are characteristic components of gross congenital malformations, insufficiency of otherwise normal orifices seems to be a less specific finding. The possible significance of such insufficiency in infancy and childhood is

... a condition that may be separately or jointly involved in orificial insufficiency. The present paper is concerned with the appearance of ducts in the various lobes of the prostate and other prostatic channels at roentgenography.

*Material and Methods.* The material comprised a series of 47 boys in whom contrast medium had on one or more occasions entered ducts of the prostate.

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proper at micturition urethrocytography. Various other channels in the prostate were also demonstrated in some of the boys. Three additional boys, in whom a similar examination had failed to demonstrate any ducts of the prostate proper, were included to augment the differential diagnosis. The age of the boys investigated ranged from less than 1 day to 15 years.

Urethrocytography was performed by the technique described by RUDIE (1964). The roentgenograms obtained during micturition included a p views with a vertical roentgen ray beam and with the beam tilted  $15^\circ$  cranially and at least one lateral view and sometimes oblique views of the urethra. The films were evaluated by comparison with available anatomic descriptions of the normal inner structure of the prostate, and the ducts demonstrated were as far as possible assigned to the respective prostatic lobes.

### **Development and anatomy of the prostatic channels**

The normal development of the prostate gland in human fetuses has been described in detail by LOWSLEY (1912, 1915). This starts at the third month of intra-uterine life with the appearance of solid epithelial buds, which emerge from five distinct areas in the posterior part of the urethra. The buds ramify and become hollow, and at the 16th week muscle fibres appear around the resultant tubules. Further development is characterized mainly by the growth of these epithelial and muscular elements, by the formation of an enclosing fibrous capsule, and by the appearance of a collicle, the verumontanum, at the site where the Wolffian and Mullerian ducts open on the posterior wall of the urethra.

One of the original five groups of tubules undergoes marked atrophy before birth, while the others steadily increase in size and number of branches. The various groups thereby approach each other but, their growth not being uniform, the parts of the prostate gland that they compose become unequal in size. Behind the urethra the gland surrounds the derivatives of the Wolffian and Mullerian ducts, i.e. the ejaculatory ducts and the utricle, which are enveloped in a separate capsule. After birth the gland grows slowly until puberty, at which time it again rapidly increases in size. Growth then continues at a lower rate, and the maximum size is reached during the third decade. Any later enlargement is considered abnormal and due to hyperplasia or other pathologic changes.

#### *The utricle*

While the two Mullerian ducts in the male fetus practically disappear, their cloacal ends persist and become converted into pockets in and behind the posterior wall of the urethra. Their lumina may remain separate, giving rise to a large utricle divided into two compartments by a median septum. Usually,



Fig 1 Wax model of prostate of newborn Dorsal aspect L L lateral lobe, P L posterior lobe, S V seminal vesicle, U urethra Bold line indicates border of P L (Modified after LOWSLEY 1912)

however, the pockets fuse and persist merely as a narrow undivided utricle which averages only 4 mm in length. The orifice is situated in the midline at the highest part of the verumontanum, it is usually round and in childhood less than 1 mm in diameter. The range of variation is, however, considerable, and an undivided utricle is not infrequently 2 to 3 mm in width and several millimeters in length. It then extends in a cranial direction behind and parallel to the urethra, and its orifice may be a longitudinal slit. The utricle and its orifice seem to increase in size only slightly after birth.

#### *The ejaculatory ducts and seminal vesicles*

A major part of each Wolffian duct in the male fetus forms the vas deferens and the ejaculatory duct and in the 13th week produces a lateral evagination, which develops into the seminal vesicle. The vesicle contains a varying number of characteristically convoluted tubules and a tortuous main duct, which joins the vas deferens at or within the base of the prostate. The ejaculatory duct extends from this junction obliquely through the prostate towards the upper part of the verumontanum and then proceeds close to the midline parallel to the lumen of the urethra. The two orifices of the two ejaculatory ducts are situated lateral to that of the utricle, usually somewhat above it but occasionally below it.

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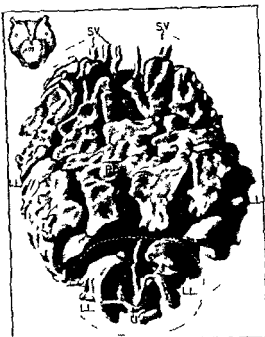


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Fig 2 Wax model of prostate of newborn Median aspect (left half of model) A L anterior lobe, A T Albarran tubules, B I bladder, E J ejaculatory duct, L L lateral lobe L U r left ureter, M L middle lobe, P prostate gland P L posterior lobe S V seminal vesicle U urethra, U P utricle Bold lines indicate borders of M L and P L (Modified after LOWSLEY 1912)



The seminal vesicles grow backward and laterally, at birth they may almost reach the base of the trigone of the bladder. Growth continues during the period of adolescence, and adult size is reached in the third decade. The ejaculatory ducts increase in length with the growth of the verumontanum.

### *The ducts of the prostate proper*

Throughout its development the prostate maintains the original feature of being composed of five separate epithelial parts. The branching tubules of these parts change relative to each other, but the branches of different parts do not intermingle and the urethral orifices of the tubules remain grouped within fairly distinct areas. In contrast with the exterior of the fully developed gland the architecture of the ducts clearly indicates that the prostate is persistently made up of as many as five lobes, viz. the anterior lobe, the middle lobe, the right and left lateral lobes, and the posterior lobe (Figs 1 and 2).

The anterior lobe atrophies before birth and then normally remains relatively insignificant in size throughout life. It contains a small number of short ducts, which open into the urethra in the upper part of the anterior wall.

The middle lobe may be absent but usually occupies the space between the supracollicular segment of the urethra and the ejaculatory ducts. Its tubules, about ten in number, open on the sides of the upper part of the verumontanum. Some of their branches may extend behind and up to the superior border of the vesical sphincter.

The lateral lobes compose the main part of the base of the prostate. They are separated by the middle and posterior lobes and by the ejaculatory ducts and the utricle. Their ducts are larger and more numerous — usually more than thirty —



Fig 3 Age 1 1/2 years Ap and lateral views Duct in anterior prostatic lobe Narrow utricle

than those of the other lobes. They open on the lateral walls of the urethra and in the furrows along the sides of the verumontanum and extend in posterior and lateral directions towards the base of the bladder. In the apex of the prostate, however, some of the ducts send branches in a forward direction, these branches approach those of the other lateral lobe anterior to the urethra.

The posterior lobe makes up the major part of the apex of the prostate. It lies below the ejaculatory ducts and behind the urethra and is separated from the lateral lobes by a fibrous capsule. Its terminal ducts average only eight in number but branch extensively, extending dorsad towards the bladder from their orifices, which are situated in the posterior wall of the urethra below those of the ejaculatory ducts and utricle.

The branches of the lobar prostatic ducts are exceedingly numerous. They are ordinarily tiny and fairly uniform in size. A duct, which opens into the urethra, branches into many tubules, all of which are similar in width to the terminal duct; they jointly form the total number of orifices of prostatic ducts in the urethra is more than fifty and may even exceed seventy.

*Periurethral ducts* The prostatic part of the urethra is the site of numerous mucous and submucous secreting tubules usually referred to as the periurethral, or internal, glands of the prostate. These open into the urethra alongside the ducts of the prostate proper.

#### *Accessory ducts*

In addition to the tubules of the prostate proper and of the prostatic part of the urethra there are two normal groups of accessory ducts at somewhat higher levels, viz the subcervical (Albarran's) tubules and the sublingual (Home's) tubules.



Fig 4 Age 11 years Ap and lateral views Ducts in anterior and presumably both lateral prostatic lobes

The former are situated behind the urethra in the lower half of the vesical sphincter and open on the posterior wall of the urethra above the verumontanum, whereas the latter belong to the mucosa of the trigone of the bladder. Both groups form small subsidiary glands, which are outside the capsule of the prostate but which may, like the prostate proper, become hyperplastic. In childhood these accessory ducts are only short and their orifices extremely small.

#### *Anomalous ducts in the prostate*

Certain malformations of the genito-urinary system may result in anomalous channels piercing the prostate and opening into the urethra. The commonest of these anomalies are ectopic ureters and ano-rectal agenesis.

An *ectopic ureter* with or without ureterocoele and with or without connexion with functioning renal tissue may open into the urethra in either sex. The course of its lower segment and the site of its orifice vary, but being developmentally bound to the Wolffian duct the ureter in the male cannot, according to Kjellberg et coll (1957), open into the urethra at a level lower than that of the verumontanum.

In *ano-rectal agenesis* a narrow communication may extend between the bowel and the urinary tract. This so-called fistula, which is probably the actual terminal segment of the anomalous rectum, may in the male open into the prostatic or the diaphragmatic part of the urethra or, rarely, into the urinary bladder. Its urethral orifice is in the posterior wall, which may be more or less acutely kinked by the traction exerted by the ectopic rectum (Rudhe 1968).



Fig 5 Age 11 days A p and lateral views  
Ducts in middle and presumably right  
lateral prostatic lobes Small utricle

## Results

*Ducts of the prostate proper* were evident at urethrocystography in 47 cases, which was, as mentioned, the criterion used for acceptance in this series. The visible ducts ranged in number from only one to virtually all macroscopically discernible ducts in the gland. They usually appeared as less than 1 mm wide and 1 to 5 mm long, straight or slightly curved tubules with or without branches. The ducts were however as wide as 2 to 3 mm in their peripheral parts in 2 patients. The orifices were usually obscured by the contrast medium in the urethra in all views obtained and could therefore only rarely be located precisely.

The distribution of visible ducts in 32 boys permitted identification of the affected lobe or lobes, whereas in the remaining 15 boys, in whom only a few ducts were demonstrated and visible only in the a p views, it could not be decided with certainty whether these belonged to a lateral or to the posterior lobe. The contrast medium passed far peripherally in the prostate via a large number of minute ducts in 18 patients and appeared to fill the parenchyma onto the capsular border of the gland. The position and shape of such regions helped recognition of the lobe or lobes involved.

Ducts were located in the anterior lobe in 2 boys (Figs 3 and 4). In the lateral view they were seen to extend from the uppermost part of the urethra a few millimeters in a forward and slightly upward direction parallel to and close to the anterior wall of the urinary bladder, they were not visible in a p views. In one of these patients the utricle and, in the other a few tiny ducts in the lateral lobes, were demonstrated simultaneously.

Ducts in the middle lobe were recognized in only one patient (Fig 5), and in the lateral view extended from the upper part of the verumontanum backwards and upwards in a small region, which appeared to be filled with contrast medium in the urethra. The ducts were also discernible in the a p tilt view despite over-

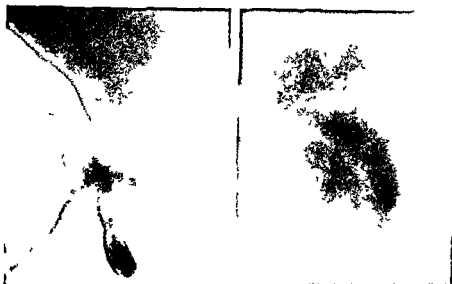


Fig 6 Age 7 1/2 years Ap and lateral views Catheter in urethra Posterior and both lateral prostatic lobes filled with contrast medium

lapping of contrast medium The utricle and a duct supposed to belong to the right lateral lobe were also visible in this instance

Ducts in the lateral lobes were identified in 29 cases, including 19 with complete or partial loading of one or both of these lobes Both lateral lobes were affected in 23 boys, only the right lobe in 3, and only the left lobe in 4 boys In



Fig 7

Fig 7 Age 17 days Ap and lateral views Upper part of lateral prostatic lobes filled with contrast medium

Fig 8 Age 9 1/2 years Slightly oblique view Upper part of lateral prostatic lobes filled with contrast medium Mucosal urethral folds on left side extending upwards from verumontanum



Fig 9 Age 23 days A p and oblique views Reflux to dilated ureters Urethra markedly dilated down to obstructing valve Posterior prostatic lobe filled with contrast medium

6 of these 29 cases ducts were also evident in the anterior, middle, or posterior lobe, and in 4 patients the utricle was also visible

When only terminal tubules were demonstrated in the lateral lobes, they were visible in the a p and oblique views but not in the lateral view, they usually appeared to extend from the urethra in a cranio-lateral, though rarely in a purely lateral, direction Filling with contrast medium in 5 cases affected the entire lateral lobes and thus included their preurethral parts, which proved to be considerably larger than the anterior lobe (Fig 6), the lateral lobes were also seen to extend far laterally and backwards and were visible in all the views Filling was limited to the upper part of one or both lateral lobes in 9 cases This part was recognized in the a p and oblique views by its somewhat pointed cranio-lateral pole and its mediad slope towards the midline behind the urethra (Figs 7 8 and 11)

A few ducts evident in the a p views in a further 15 cases on one or both sides of the urethra were probably situated in the lateral lobes but, as mentioned, may have belonged to the posterior lobe (Figs 4 and 5)

Multiple ducts were present in the posterior lobe in 7 patients In all of these the posterior lobe appeared filled with contrast medium, and in all except one such filling also occurred in one or both lateral lobes The lateral borders of the posterior lobe were projected outside the urethra in the a p views and the upper border crossed the midline transversely behind the urethra (Figs 6 and 9) The backward extension of the posterior lobe was difficult to evaluate because of overlapping of the lateral lobes in the lateral and oblique views In the one boy in whom the posterior lobe was separately affected the urethra was markedly dilated down to a severely obstructing valve and in the lateral view almost entirely concealed the ducts demonstrated (Fig 9)



Fig 12



Fig 13

Fig 12 Age 10 months Ap and lateral views Left sided ectopic supernumerary ureter piercing prostate Paraosteal diverticulum at orifice of orthotopic left ureter

Fig 13 Age 3 months Ap and lateral views Duct like collection of contrast medium in furrows along verumontanum Minute diverticulum in bulbous part of urethra (arrow)

tures in newborns and despite the inevitable overlapping of bone in some or all views in the highest age groups. On the other hand, if only a few such channels are visible, they may be difficult to locate precisely since they are often not demonstrable in all views obtained and since their orifices can only rarely be discerned. These difficulties may occasionally even cause misinterpretation of mucosal furrows in the urethra as minor prostatic ducts.

Truly anomalous channels in the prostate are readily distinguished from ordinary ducts if seen to convey contrast medium to the bowel or to the upper urinary pathways. A fistula between the urethra and the bowel may, however, temporarily be partly occluded (RUDHE 1968) and thus at urethrocytography resemble an intraprostatic or subprostatic cul-de-sac. The marked postoperative widening of a fistula stump following ligation and transection, as evident in one of the present cases, seems to be unusual although similar appearances have been reported by CURRARIO (1969). An ectopic ureter piercing the prostate may, as exemplified above at urethrocytography, present only its short intraprostatic segment. A postoperative remnant of such a ureter may be confined in its entirety to the prostate. Additional information obtained from other types of examinations and the history will usually disclose the true nature of the channel in these cases.

Of the ordinary prostatic channels, the ureter may differ radiographically in shape as well as in size from one case to another (EHLING 1950) but is recognizable from its median position; the ejaculatory ducts can be identified by their almost median site and slightly oblique course. An ejaculatory duct may, however, as exemplified above, empty during the examination and thus be visible,

for example, in lateral but not in a p views, in the former it resembles a utricle, for which under these circumstances it may be mistaken unless contrast medium is also present in the seminal vesicle. The tendency of the latter to retain contrast medium longer than the ejaculatory duct helps to prevent such mistakes.

The ducts of the prostate proper differ in appearance in various views according to their lobar distribution and may therefore, if visible in sufficient number, be radiographically located to individual lobes. Filling of the parenchyma with contrast medium via these ducts may demonstrate the size and shape of the corresponding region of the gland and thereby help to identify the lobes. If but few in number, visible prostatic ducts may be recognized as such but only rarely be assigned with certainty to a specific lobe.

## SUMMARY

The radiographic appearance of prostatic channels was investigated in micturition urethrocytograms obtained in 50 male infants and children. The visible channels, which included ordinary as well as certain anomalous structures, were assessed in the light of available anatomic descriptions. Ducts of the prostate proper were demonstrated in 47 patients and in 32 of these could be assigned to specific lobes.

## ZUSAMMENFASSUNG

Das Röntgenbild der Prostatagänge bei Miktionsurethrozystographie wurde an 50 männlichen Säuglingen und Kindern studiert. Im Lichte verfügbarer anatomischer Beschreibungen wurde festgestellt, dass die sichtbaren Gänge als auch die der Prostata selbst zugeordnet werden können.

## RÉSUMÉ

L'auteur a examiné l'image radiographique des canaux prostatiques sur des urethrocytogrammes mictionnelles de 50 garçons nourrissons et enfants. Les canaux visibles qui comprennent des structures normales et certaines structures anormales ont été examinés à la lumière des descriptions anatomiques existantes. Chez 47 patients l'auteur a mis en évidence des canaux prostatiques proprement dits et chez 32 de ces sujets il a pu les attribuer à des lobes prostatiques déterminés.

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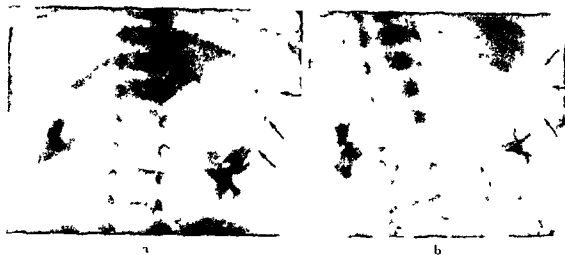


Fig 1 Operatively verified asymptomatic adrenal haematoma in an 8 day old boy. Unimpaired excretion of contrast medium at urography. Displacement of the left kidney mainly downwards and outwards with slight lateral rotation of the cranial pole (a). Accumulation of contrast medium peripherally in the expansive process during nephrographic phase of excretion (arrows) (a and b).

The mothers of the two smallest babies, both boys, were successfully treated for impending abortion during the last month of pregnancy by the administration of a compound (Duvalidan), chemically known as isosuprine chloride. The smallest baby was delivered by caesarean section because of three previous still births caused by complications during labour. Delivery was uneventful in the second of these two cases. Pregnancy and confinement were undisturbed in the two remaining cases.

None of the babies displayed any signs of disease apart from the finding of a mass on routine palpation of the abdomen performed in the maternity ward on the 1st, 8th, 4th and 4th day of life, respectively. It uniformly gave the impression of a limited, almost solid process inseparable from the adjacent kidney. The lesion was left-sided in three of the babies, and right-sided in one.

**Röntgen findings** These were essentially identical in all 4 cases. Excretion of the contrast medium at urography was unimpaired. Detailed outlining of the cranial pole of the kidney was not possible adjacent to the expansive process, this was true in the conventional abdominal films as well as in those exposed during the nephrographic phase of excretion (Fig 1 a). In two of the subjects, early nephrograms revealed a slight accumulation of contrast medium along the periphery of the expansive process (Fig 1), producing an effect similar to that occasionally obtained in hydronephrosis (Fig 2 a). The kidney ipsilateral to the palpable mass was displaced mainly caudally in all 4 subjects. In two of them,



Fig 2 Renal duplication with low top c ureter in an 8  
mulat on of contras  
upper renal pole (ar  
the wide correspond

however slight lateral displacement with minor outward rotation of the kidney were also present (Fig 1 a). Compression of the renal pelvis was suggested in 3 of the cases the mass

3) No  
of the c

*Surgical findings and biopsy* Operative exploration of the retroperitoneum revealed a large typical adrenal haematoma in two of the subjects. The haematoma was evacuated and drained with the suprarenal gland left in situ. In the other two cases a reliable diagnosis was hard to make from the appearances of

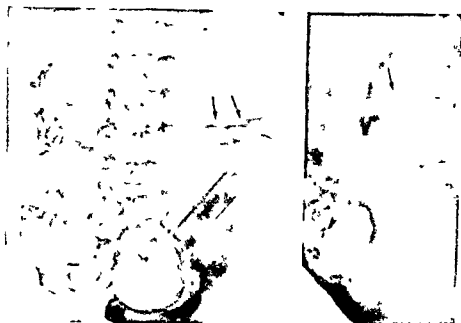


Fig 3 Operatively verified asymptomatic adrenal haematoma in a 1 day old boy. Displacement of the left kidney mainly downwards. Compression and stretching of renal pelvis and some calyces (arrows)

the process on exploration. The masses were therefore extirpated together with tissue that on microscopic examination appeared to be composed of partly destroyed suprarenal glands. Fresh and older haemorrhages, suggestive of repeated minor bleedings, formed the actual haematomas. Microscopy revealed a rim of thin calcifications in the remnants of the superficial cortical layers of the extirpated part of the adrenal in the one of the latter patients.

### Discussion and Conclusions

The relative size of the suprarenal glands of the newborn infant strikingly exceeds the dimensions present during adolescence and adult life. Due to the involution of the foetal cortex, which begins immediately after birth, the average combined weight of the adrenals is reported to decrease by about a half during the first months of life (TAMURA 1951). During this period the adrenals are intensely hyperemic, a state sometimes erroneously interpreted as caused by interstitial bleeding. In fact, true haemorrhage, and particularly massive bleeding is an uncommon event (BROWN et coll 1962, GLENN 1962), haemorrhage when demonstrated should always be regarded as pathologic (POTTER 1953).

The pathogenesis of adrenal haemorrhage of the neonate is still inadequately understood. Most authors quote asphyxia at birth, resulting in venous congestion,

or trauma during delivery or at postnatal resuscitation, as being the main etiologic factors (MARIN et coll 1955, HILL & WILLIAMS 1958, BUCH & THANDRUP 1961, GLENN 1962, BROWN et coll 1962 and others) Premature babies, large infants and babies born to diabetic mothers are said to be more susceptible than others (SOBER & HIRSCH 1965, SOMMERSCHIED 1970) Severe maternal infection and haemorrhagic disorders are mentioned as contributory factors (HILL & WILLIAMS, BUCH & THANDRUP, BROWN et coll) Adrenal haemorrhage also occurs more frequently during the first postnatal week, when hypoprothrombinemia and increased vascular fragility are particularly marked (MARIN et coll 1955)

There seems to be no report available of imminent but successfully treated abortion leading to an adrenal haematoma diagnosed after birth Although the connection between this potential cause of bleeding and the adrenal haemorrhages appearing in the two first mentioned cases is far from proven, it cannot be completely excluded A transient period of asphyxia during the last month of gestation might have been capable of eliciting the actual lesion just as well as asphyxia during labour It is not felt that the drug used (Divaldan) should be incriminated since no side effects on the human foetus have been reported (SJOBLOM 1970)

Pregnancy as well as labour were uneventful in the third and fourth cases but the weight of these neonates was clearly above the average

The affected adrenal may be permanently destroyed by massive bleeding (GLENN) The haematoma may rupture through the capsule to produce a large retroperitoneal mass, occasionally the rupture may occur into the peritoneum (HILL & WILLIAMS, BROWN et coll) Huge bilateral haemorrhages are considered to be inevitably fatal even in unilateral bleeding with rupture of the capsule the prognosis is dubious The general effects are alarming with collapse, pallor and dyspnoea Replacement of the blood loss is urgent, and immediate laparotomy is usually indicated The fact that normal neonatal adrenals excrete only small amounts of steroids during the first week of life, probably accounts for the low incidence of adrenal insufficiency in haemorrhage of the gland (GLENN)

A moderate haemorrhage, just as repeated small bleedings, tends to remain intracapsular The course is then mostly benign Small haematomas may resolve completely or the haematoma may rapidly undergo organisation and calcify (GROSS et coll 1967) Calcifications are occasionally found in the suprarenal gland as early as a few days after birth although they are usually incidental findings at conventional roentgen examinations of the abdomen and remain undetected until childhood, adolescence or later during adult life The evolution of such calcifications from clinically acute or subacute adrenal haemorrhage has been roentgenologically demonstrated by KAPLAN et coll (1964) and LORBER (1965)

The occasional finding of a suprarenal calcification in the absence of an expansive process, according to JARVIS & SEAMAN (1959), and in the experience of the present author is more common in childhood. The absence of a mass supports the diagnosis of a calcified renal haematoma. However, this feature is not diagnostic since a neuroblastoma may be very small when discovered. Furthermore a calcified haematoma may displace the kidney and simulate a neoplasm (WILLIAMS 1956).

SOMMERSCHIELD (1970) stated that only 13 fully verified and successfully treated cases of adrenal haematoma presenting with a palpable mass as the single clinical manifestation have been recorded to date. The present report adds 4 cases.

Apparently no physical sign, laboratory investigation nor roentgen examination can be considered as diagnostic in adrenal haemorrhage. The roentgenologic features in the present series fail to distinguish themselves from those present in neonatal neuroblastoma, although the accumulation of contrast medium along the periphery of the mass as demonstrated in two of the cases would appear to be highly suggestive of a haematoma. This feature may reflect the events taking part in 'total body opacification' (O'CONNOR & NEUHAUSER 1963) following a large dose of intravenously injected contrast medium. The roentgen appearances were somewhat similar to those in renal duplication with impaired emptying of the heterotopic renal pelvis or the corresponding ureter (BERDON et coll 1968) (Fig 2a). Prolongation of the urography in the present cases with exposure of late films failed to reveal a supernumerary pelvis, contrary to the commonly successful demonstration of the dilated renal pelvis in hydronephrosis (Fig 2b). Nevertheless, the presence of a neuroblastoma, stated to be uncommon in newborn infants (BERDON & BAKER 1969), has to be considered as an alternative until proved otherwise. At least one case of clinically asymptomatic adrenal haematoma and neuroblastoma involving one and the same suprarenal gland is on record (SOBER & HIRSCH 1965). The diagnosis was established on histologic examination alone. A retroperitoneal expansive process with displacement of the kidney downwards and outwards, concurrent rotation of the kidney and a renal pelvic deformity in the form of stretched and compressed calyces must therefore confuse the ultimate roentgenologic diagnosis in this age group. So far there are no reports on angiographic examinations convincingly contributing to the diagnosis of adrenal haematoma in the neonate.

Displacement of the kidney, and deformity of the renal pelvis similar to that present in three of the present cases, may be evident in renal pelvic duplication when the corresponding ureter ends ectopically, with or without a ureterocele (BERDON et coll 1968). The demonstration of a ureteral or a bladder deformity is of course diagnostic in these cases.

The repeatedly reported occurrence of a non functioning kidney (HUGHES & WILLS 1965, SOMMERSCHILD 1970) on the side of the adrenal haematoma is usually attributed to thrombosis of the renal vein or the inferior vena cava. However, in the absence of renal function on the affected side, hydronephrosis, multicystic kidney, nephroblastoma and even neuroblastoma are other possibilities that have to be considered in the differential diagnosis.

An asymptomatic retroperitoneal mass in a newborn baby should invariably call for surgical exploration. A conservative attitude is less recommendable as malignancy cannot be excluded. If the mass is caused by haemorrhage of the adrenal gland, evacuation of the field often appears to be a satisfactory approach. If, however, the operation leaves doubts as to the nature of the mass, its extirpation should be the method of choice.

### SUMMARY

The roentgen features in 4 recently observed cases of large asymptomatic adrenal haematomas of the neonate are analyzed and the differential diagnosis is discussed. Physical signs, laboratory investigations and roentgenologic examinations are usually inconclusive as regards the actual nature of the process. Surgical exploration is therefore nearly always indicated.

### ZUSAMMENFASSUNG

Es wird von 4 Neugeborenen mit grossen symptomlosen Hamatomen der Nebenniere berichtet und die Röntgenscheinungen und deren Differentialdiagnose werden besprochen. Gewöhnlich sind die Ergebnisse der klinischen und radiologischen Untersuchung völlig ohne Resultat hinsichtlich der wahren Natur der Erkrankung und auch das Laboratorium ist nicht imstande nützliche Beiträge zu liefern. Eine Diagnose kann lediglich durch chirurgisches Eingehen gestellt werden.

### RÉSUMÉ

L'auteur analyse les signes radiologiques de 4 cas observés récemment de volumineux hématomes surrenaux asymptomatiques du nouveau né et discute le diagnostic différentiel. Les signes physiques, les examens de laboratoire et les examens radiologiques ne permettent habituellement pas de conclure en ce qui concerne la véritable nature de cette affection. C'est pourquoi l'exploration chirurgicale est presque toujours indiquée.

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## ANGIOGRAPHY IN DIMETHYLNITROSAMINE-INDUCED RAT RENAL TUMOURS

by

LEIF EKELUND and NILS JONSSON

Experimental rat renal tumours, induced by dimethylnitrosamine (DMN), have been described by MAGEE & BARNES (1959, 1962), ZAR et coll (1960) and ARGUS & HOCH LICETI (1961). Angiographic investigations in vivo of experimentally induced renal tumours have not yet been reported. A method for selective catheterization of arteries in the rat has, however, recently been developed (EKELUND & OLIN 1970), and the present investigation is concerned with angiographic examinations of DMN induced rat renal tumours as an experimental model.

*Material and Methods* Twenty five white rats (*Rattus norvegicus albinus*) of Wistar strain of both sexes with a weight of 100 to 150 g at the beginning of the experiment were used. They received DMN (Aldrich Chemical, USA), dissolved in arachis oil and mixed with corn pellets, for one week, the mean total dose of DMN per rat was estimated to be 200 mg/kg. The rats were then returned to a normal diet of commercial pellets. Fourteen rats were examined by angiography at 26 to 30 weeks (group I), and the remaining eleven rats at

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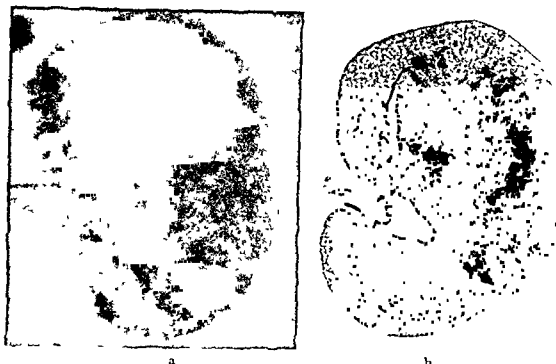


Fig 1 a) Selective nephroangiography (left) 43 weeks after DMN. Large tumour in the lateral part of the kidney with occlusion of artery centrally. b) Photomicrogram of the same kidney. Partly hyalinized tumour of anaplastic type. Htx-van Gieson  $\times 5$ .

40 to 45 weeks (group II). The catheterization was performed under general ether anaesthesia, the catheter (OPP 10, outer diameter 0.65 mm, inner diameter 0.25 mm) being introduced through the femoral artery by a cutdown technique. The technical details concerning catheterization and angiographic procedures have been described in a previous paper (EKLUND & OLIN 1970). Single magnification views were obtained at about 4 sec after the start of the contrast injection on industrial film (Structurix D 4, Agfa-Gevaert).

Following angiography, the rats were sacrificed and autopsy performed. Both kidneys were fixed by immersion in neutral formalin 10%. Sections (4  $\mu$ ) were prepared from the tumour-infiltrated kidneys corresponding to the largest tumour diameter. From kidneys without macroscopically visible tumours at least

Fig 2 a) Selective nephroangiography (right) 30 weeks after DMN. Tumour in the cranial pole of the kidney with displacement of artery. b) Photomicrogram of the same kidney with tumour in the cranial pole of anaplastic type with central hyalinized parts. Htx-van Gieson  $\times 65$ .

Fig 3 a) Selective nephroangiography (left) 41 weeks after DMN. The tumour in the cranial pole appears to be cystic, displacement of arteries with pool of contrast medium laterally. b) Photomicrogram of the same tumour (anaplastic type) with central hematomas corresponding to the areas appearing cystic in the angiogram. Htx-van Gieson  $\times 65$ .



a

Fig 2 (For legend see opposite page )



b



a

Fig 3 (For legend see opposite page )



b

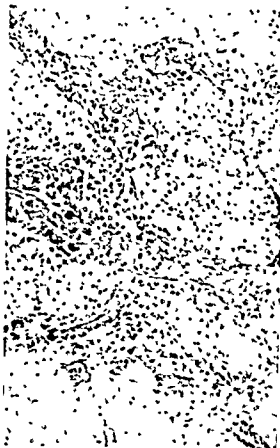


Fig 4 Photomicrogram of DMN induced kidney tumour of epithelial type Several thick walled vessels of arterial type Htx van Gieson  $\times 160$



Fig 5 Photomicrogram of DMN induced kidney tumour of anaplastic type Central partly hyalinized area with thin walled vessels of capillary or venous types Htx van Gieson  $\times 160$

six sections were examined. The sections were stained with haematoxylin-eosin and van Gieson. Special attention was paid to the vasculature of the tumour tissue and the histologic classification of the tumours.

## Results

Angiography made it possible to diagnose ten tumours, all of which were macroscopically visible, catheterization of one renal artery was unsuccessful in 3 rats. The angiographic appearances varied somewhat, especially in the degree of vascularization of the tumours, this was usually sparse, particularly in arteries (Figs 1a—3a). Veins were seldom demonstrated, possibly due to the technique employed, only single films were taken. Considerably more vessels were evident in a few tumours, especially in one instance which is not illustrated because the angiograms were unfortunately of poor quality. The central parts of some

tumours were extremely avascular, which, in at least one case, could have been due to arterial occlusion secondary to infiltration (Fig 1a) Displacement of arteries was fairly common (Fig 2a)

No significant difference in the diameter of the renal artery could be detected between tumour positive and tumour negative rats No obvious difference between the angiographic findings in group I and II could be demonstrated, except that the tumours had become larger in group II with the passage of time The histologic appearances of the renal tumours of different sizes closely corresponded to the description given by MAGEE & BARNES The neoplasms could be classified either as well differentiated and epithelial or as anaplastic and sarcoma like tumours while combinations of the two histologic types were present in a few lesions, the vascularization was different in the two types The well differentiated, epithelial neoplasms were supplied with numerous thick walled arterial vessels located in the septa of connective tissue, which separated mostly solid formations of tumour cells rich in cytoplasm (Fig 4) Thin walled vessels of capillary or venous type also occurred in these septa, as well as in the tumour lobules The vasculature of the peripheral parts of the anaplastic, sarcoma like tumours was characterized by a rich supply of thin walled vessels of capillary or venous type The central parts were often fibrous or hyalinized and contained vessels that were fewer in number and often dilated Arterial vessels were scanty (Fig 5)

Fourteen tumours were present in eleven kidneys from the 14 rats of group I examined 26 to 30 weeks after return to normal diet Seven of these growths were demonstrable only by microscopy and all the others were of small size (the largest being  $6 \times 5$  mm in section) Two of the fourteen neoplasms were well differentiated and the others anaplastic Fifteen tumours were evident in 10 kidneys from eleven rats of group II (examined 40 to 45 weeks after return to normal diet) Ten of these tumours were macroscopically demonstrable and often of considerable size, while the other 5 were microscopic and occurred in the two kidneys of one rat These 5 as well as one larger tumour were of the well differentiated type, 3 contained both histologic components, while the remaining 6 were of the pure anaplastic type

The correlation between the macroscopic tumour size and the dominating histopathologic type on the one hand and the angiographic findings on the other is given in the Table It is apparent that among the well differentiated growths all 4 which were macroscopically visible could be diagnosed angiographically while only 3 of the 9 anaplastic neoplasms were apparent in the group with a tumour diameter below 6 mm Even in the group with a tumour diameter of 6 to 10 mm one out of 3 anaplastic tumours failed to be detected angiographically (Fig 6)

Table

*Comparison between histopathologic, macroscopic and angiographic findings*

| Mean tumour diameter | Main histologic tumour type | No. of macroscopically visible tumours* | No. of angiographically diagnosed tumours |
|----------------------|-----------------------------|---|---|
| - 6 mm               | Well differentiated         | 2                                       | 2   |
|                      | Anaplastic                  | 9                                       | 3   |
| 6—10 mm              | Well differentiated         | 2                                       | 2   |
|                      | Anaplastic                  | 3                                       | 2   |
| 10 mm                | Well differentiated         | —                                       | —   |
|                      | Anaplastic                  | 1                                       | 1   |

\* Tumours detected only at microscopy are not included

### Discussion

It is obvious that selective catheterization of the renal arteries in the rat is of value in the *in vivo* investigation of experimental renal tumours. Even small-sized tumours may be diagnosed and it should also be possible to follow the growth of such neoplasms by repeated catheterization.

The vascularity of the tumour tissue is of obvious significance in the angiographic diagnosis. The two histologic types of DMN-induced rat renal tumours differed in their type of vascularization. Thus the well-differentiated tumours were supplied with numerous vessels of an arterial type against the anaplastic tumours, which contained thin-walled vessels of a capillary or venous type and poorly vascularized central parts. These differences were reflected by the greater accuracy with which the well-differentiated tumours could be diagnosed angiographically.

Whether any change occurs in the histologic or angiographic appearances with increasing tumour age cannot be concluded from the present material. (The tumours were examined a fairly short time after the DMN.)

Considering the relatively poor vascular supply, especially of the anaplastic type of tumour, phlebography of the kidney might be of value in the roentgenologic diagnosis.

A filmchanger for magnification angiography of small animals has now been constructed and with serial films it may be possible to obtain more information about the type of vascularity present in the neoplasms. It is hoped that it will be possible to investigate the development of so-called pathologic tumour vessels. Similar investigations on the possible relationship between the histopathologic and angiographic appearances in human renal neoplasms would obviously be of interest.



Fig 6 a) Selective nephroangiography (right) 42 weeks after DMN. Normal angiography. b) Photomicrogram of the same kidney. Tumour of anaplastic type in the cranial pole measuring 8 x 5 mm in the section. Hix van Gieson x 65.

## SUMMARY

Selective nephroangiography was performed in 10 of 17 rats with renal tumours induced by dimethylnitrosamine (DMN). The tumours were of two histological types: well-differentiated and anaplastic. The well-differentiated tumours showed a rich vascularization and could be diagnosed angiographically with greater accuracy than the anaplastic tumours.

## ZUSAMMENFASSUNG

An Ratten wurden mittels Abgabe von Dimethylnitrosamin Nierentumoren erzeugt und dann eine selektive Nephroangiographie vorgenommen. Zehn von siebzehn makroskopisch erkennbaren Tumoren wurden angiographisch diagnostiziert. Die zwei histologischen Tumortypen waren hinsichtlich ihrer Gefassbildung unterschiedlich, die gut differenzierten Tumoren hatten eine reichere Gefassbildung und konnten angiographisch mit grösserer Sicherheit als die anaplastischen Tumoren diagnostiziert werden.

## RÉSUMÉ

Les auteurs ont fait des angiographies renales sélectives dans des cas de tumeurs renales induites chez les rats par la dimethylnitrosamine. Sur 17 cas de néoplasie macroscopique,

ment visible ils ont pu faire le diagnostic dans dix cas. Les deux types histologiques de ces tumeurs différaient par leur vascularisation: les tumeurs bien différenciées étaient irriguées par des vaisseaux plus nombreux et ont pu être diagnostiquées angiographiquement avec plus de précision que les tumeurs anaplastiques.

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## STATIONARY WAVE OR SEGMENTAL VASOCONSTRICTION

by

ERIC BERGQUIST, UNO ERIKSON and HANS R. ULFENDAHL

Segmental, regularly arranged zones, poorly filled, may sometimes be evident within an artery at angiography. This phenomenon has been observed in the femoral artery (WICKBOM & BARTLEY 1957, THEANDER 1960, SUTTON 1962, STEINBERG 1966), the iliac arteries (SUTTON *et coll* 1963, SUTTON 1964), the carotid artery (SUTTON *et coll* 1963, SCHECHTER 1963) the renal arteries (WYLIE *et coll* 1962, SUTTON *et coll* 1963) and the superior mesenteric artery (WYLIE *et coll* 1962, MAYALL 1964, SUTTON 1964). These transverse striations have been likened to a pearl necklace (THEANDER 1960) or a bamboo rod (WICKBOM & BARTLEY 1957). The latter considered that they were caused by vasospasm, and stated that they disappeared on administration of a vasodilative agent (Priscol). SUTTON (1962) also believed the changes to be due to spasm. THEANDER (1960) observed such changes proximal to a vascular lesion at femoral angiography. He regarded them as physical phenomena and termed them 'stationary arterial waves'. These 'standing waves' were of low amplitude and short wavelength in narrow arteries, in larger arteries the amplitude seemed to be broader and the wavelength longer.

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MAYALI (1964) from experimental investigations with Urografin and water flowing in separate layers in a tube presented the theory that standing arterial waves were due to rippling of the interface between the upper layer of blood and the lower layer of contrast medium; slipping occurred between these two layers due to their different rates of flow, causing rippling. MAYALL (1966) in similar experimental investigations reported that standing waves could be demonstrated more simply by allowing turpentine to represent blood. Turpentine and Urografin 60 % were poured into a tube. When the tube was held horizontally, two distinct layers were formed, with the turpentine above the Urografin. With the tube slightly tilted the heavier Urografin ran under the upper layer towards the lower end of the tube, but the interface remained smooth. A sharper angle of tilt produced more rapid flow with rippling of the interface. These ripples increased in both length and amplitude when the experiment was repeated with increasing angles of tilt. With a steep, rapid tilt, turbulence occurred with temporary mixing of the two layers. Similar experiments with a narrower tube produced the same phenomenon but the waves were of smaller amplitude and shorter wavelength. This observation corresponded with the demonstration by THEANDER (1960) that standing waves had a short wavelength and a low amplitude in narrow vessels. MAYALL concluded that if the standing waves occurred in the same way as in his experiments, then in lateral angiograms with a horizontal beam the upper surface of the layer of contrast should be wave-like. This has not yet been observed. ISHIKAWA et coll (1967) called this phenomenon 'accordion-like shadows' in the angiogram. The 'waves' appeared inconsistently and sometimes disappeared at the next examination, they were more often apparent when femoral angiography was performed under spinal anaesthesia. These authors concluded that the changes were caused by longitudinal alternating constriction of elastic and spastic arterial wall segments.

SCHUCHTER (1963) reported that standing waves in percutaneous carotid catheterization disappeared when the catheter was slightly withdrawn and a further injection of contrast medium was made. He considered this to be evidence that the waves were not of an organic nature. WYLIE et coll (1962) occasionally observed multiple regularly-spaced constrictions in the mesenteric or peripheral arteries, which occurred after the rapid injection of a large volume of concentrated angiographic medium. The subsequent injection of a weaker solution failed to produce such irregularities. These authors felt that the concentration and amount of contrast medium were deciding factors in the occurrence of standing waves. ERIKSON (1965) had 6 patients with these appearances in a series of 101 patients with posttraumatic leg amputation subjected to angiography.



Fig 1 Case 1 a) Segmental contractions in the anterior tibial artery b) Similar phenomenon one year later in the popliteal artery after a below knee amputation



Fig 2 Case 2 Angiogram without previous injection of a vasoactive drug Segmental contractions in the superficial femoral artery (a) not present after the intra-arterial injection of bradykinin (b) acetylcholine or histamine

The hypotheses on the origin of such standing waves are thus numerous, and none of them has been verified to date. Some theories are based on physical explanations, and others on the assumption that the waves are induced by spasm. It is generally considered that the waves are of a harmless nature.

The following are reports of 4 patients in whom angiography was performed on repeated occasions and in whom segmental contractions were observed. Similar contractions occurred in experiments with latex casts in rabbits; these increased in number and intensity with an augmented tone of the vessel wall.

### Case reports

**Case 1** Male, aged 27, who had been examined with angiography one year before and following below knee amputation. In both examinations 20 ml Urografin 60% were injected manually through a needle. Serial angiograms with a frequency of one frame per second were recorded. At the second angiography the blood flow in the stump, as measured by venous occlusion plethysmography (ERIKSON 1963, GRAF 1964), was 2.8 ml/100 ml $\times$ min and at the same level in the intact leg was 3.0 ml/100 ml $\times$ min.



Fig 3 (For legend see opposite page )



Fig 4 Case 3 a) Selective angiography of the left renal artery. The lower branches of the artery have irregular, undulatory contours (back flow of contrast medium to the aorta) b) Selective angiography of the left renal artery after a 10 min infusion of 10  $\mu\text{g}/\text{min}$  bradykinin. The irregularities observed in the lower branches of the artery before the bradykinin infusion now absent, (no back flow of contrast medium to the aorta)

**Case 2** Male, aged 21, posttraumatic above knee amputation. Angiographies of the amputation stump were performed by percutaneous femoral catheterization in the third week after operation. The same amount of contrast medium and exposure frequency were used as in Case 1. (1) intact leg, (2) after a 10 min intraarterial injection of 10  $\mu\text{g}$  histamine (blood flow 100  $\text{ml} \times \text{min}$ ), (3) after a 10 min intraarterial injection of 9  $\text{mg}/\text{min}$  acetylcholine (blood flow 15.6  $\text{ml}/100 \text{ ml} \times \text{min}$ ) and (4) after a 10 min intraarterial injection of 10  $\mu\text{g}$  histamine (blood flow 8.3  $\text{ml}/100 \text{ ml} \times \text{min}$ ). The patient was in good clinical condition. The values for blood sedimentation rate, haematocrit and red and white blood cells were normal, the blood pressure and ECG were also normal.

**Case 3** Male, aged 20, who had had an adenoma of the cortex of the left adrenal gland removed. Abdominal aortography and three selective angiographies of the superior me-

Fig 3 Case 3 a) Lumbar aortography. Slightly irregular undulatory wall contours or segmental contractions present bilaterally in the lower renal arterial as well as in the more peripheral branches of the superior mesenteric artery. b) Irregular undulatory wall contours are also present in both the main branches of the superior mesenteric artery.



Fig. 5 Case 4 a) Segmental contractions at angiography before injection of bradykinin b) These disappeared after bradykinin but c) re appeared at the third angiography when no bradykinin had been given

senteric artery and left renal artery were performed. The aortography was carried out with 40 ml Urografin 60% and the selective angiographies with 15 ml Urografin 60% a pressure syringe at 4 kP/cm was used. The exposure frequency was three frames per second for three seconds followed by one per second for six seconds. The second of the three selective angiographies in the two different arteries was preceded by a 10 min injection of 10  $\mu$ g/min bradykinin.

*Case 4* Male aged 40 with intermittent claudication due to occlusion of the femoral artery in adductor canal. Three angiographies by the percutaneous femoral technique were performed. 20 ml Urografin 60% being injected with a pressure syringe at 5 kP/cm. The exposure frequency was one frame per second. The second angiography was preceded by a 10 min intrarterial injection of 10  $\mu$ g/min bradykinin. No vasodilative drugs were given before the first and third examinations.

### Experimental investigations

The purpose of the animal experiments was to investigate the influence of increased vasomotor tonus on the configuration of the arterial wall. Ten adult rabbits were anaesthetized with Nembutal and a polythene catheter was intro-



Fig 6 a) Cast of renal arterial branches after weak stimulation of splanchnic nerve, minor contractions evident b) Detail of arterial cast in renal cortex after strong stimulation of splanchnic nerve. Vascular constriction marked with arrow

duced into the abdominal aorta. Different degrees of vascular spasm were induced by electrical stimulation of the splanchnic nerves. The catheter was connected to a 5 ml syringe filled with a latex solution, which was injected at a pressure of about 250 mm Hg. During the injection the aorta was clamped cranial to the renal arteries, as were the large intestinal arteries. One minute after the injection the renal pedicles were ligated. The kidneys were removed and placed in concentrated hydrochloric acid overnight and then washed with tap water. The latex casts of the renal vascular tree were studied microscopically and photographed.

### Results

The first case (Fig 1) had segmental contractions in the two investigations carried out at an interval of one year. In the second case the same phenomenon was noted in the superficial femoral artery but disappeared after the intra-arterial injection of different vasodilative agents (Fig 2). The third case (Figs 3 and 4) had segmental contractions of the renal and superior mesenteric arteries similar to those encountered in fibromuscular hyperplasia. These relaxed after the injection of bradykinin but again appeared at the third angiography when no vasoactive drugs had been administered. The fourth case presented (in the superficial femoral artery) the same reactions as Case 3 (Fig 5).

The casts of the vessels had typical circular constrictions following the previous weak low-frequency stimulation. The appearances were present in both the small and larger arteries. The result of weak stimulation is reproduced in Fig. 6a. The circular constrictions on high intensity stimulation were frequent and sometimes totally obstructed the arteries (Fig. 6b). Only few arteries had a tendency to spastic circular constrictions in kidneys without nerve stimulation.

### Discussion

The clinical results indicated that the phenomenon which is referred to by terms such as segmental spasm and standing waves may occur within different vascular regions and be produced by different techniques, e.g. injection with a needle or catheter either with a pressure syringe or by hand. These constrictions occurred regardless of whether the contrast medium was injected into the aorta or selectively into other arteries. The effects disappeared when the vascular region was influenced by bradykinin, histamine or acetylcholine, but returned in the 2 patients in whom the investigation was repeated without the preceding injection of such drugs. These results may indicate that the phenomenon comprises a segmental contraction of these arteries that can be influenced by vasodilative agents. It is conceivable that the condition may be induced by the needle or catheter, or the contrast medium and also that it is an abnormal physiologic state in certain subjects. The presumably prolonged contraction might lead to an anatomic alteration of the arterial wall, which in turn might be a precursor to fibromuscular hyperplasia or similar arterial lesions. It is possible that an imbalance might arise in the nervous vasoregulatory system, perhaps with a tendency to vascular diseases.

The segmental contractions present in the latex casts greatly resembled the contractions evident at the angiographies. The increased tendency to circular contractions with increase of vascular tonus corresponds with the disappearance of the contractions in the human investigations when vasodilative agents were given. There is thus reason to believe that the irregularity in both the human examinations and the animal experiments was induced by a constriction in the vessel wall and not by a standing wave phenomenon.

ROTHFIELD (1969) discussed possible causes of fibromuscular hyperplasia, but did not include spasm among them. According to the above reasoning such an aetiology could be possible, even though little is known as yet about causes of spasm and the reactions in different individuals. It would seem conceivable that the physiologic changes known as standing waves could be included among the causes of fibromuscular hyperplasia, possibly due to prolonged contractions. This hypothesis does not appear to have been advanced previously.

## SUMMARY

Arterial segmentation at angiography may be made to disappear by the intraarterial infusion of vasodilators. Theories as to the possible causes of the phenomenon are advanced. It is suggested that also the abnormality may possibly be a precursor of fibromuscular hyperplasia or similar arterial lesions.

## ZUSAMMENFASSUNG

Es ist möglich mit Hilfe einer intra arteriellen Infusion von Vasodilatoren die arterielle Segmentierung bei der Angiographie zum Verschwinden zu bringen. Theoretischen Erklärungen für das Auftreten dieses Phänomens werden vorgelegt. Es scheint, dass diese Abnormalität ein Vorsignal für das Entstehen einer fibromuskulären Hyperplasie oder ähnlichen arteriellen Erkrankungen darstellt.

## RÉSUMÉ

L'injection intra artérielle de vasodilatateurs peut faire disparaître la segmentation artérielle qui apparaît à l'angiographie. Les auteurs avancent diverses théories pour expliquer ce phénomène. Ils pensent que cette anomalie peut être un précurseur de l'hyperplasie fibromusculaire ou de lésions artérielles semblables.

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## DIAGNOSIS OF GASTRIC VARICES BY CONVENTIONAL ROENTGENOGRAPHY AS COMPARED WITH SPLENOPORTAL PHLEBOGRAPHY

by

NILS GABRIELSSON

Haemorrhage from gastrooesophageal varices is a severe complication of intra- and prehepatic obstruction. The treatment of choice is tamponade, injection of sclerosing solutions, ligation or resection of varices and shunt surgery. Localization of the bleeding varix is important in the treatment. Diagnostic procedures have been focussed on recognition of oesophageal varices since they are more easily demonstrated and considered to induce bleeding more often than gastric varices (LIEBOWITZ & ROUSSELOT 1959).

Gastric varices were first diagnosed at autopsy in a case of portal vein thrombosis (FRERICH 1861). Several cases of gastrointestinal haemorrhage in which varices of the gastric fornix, evident at autopsy, were the probable cause of bleeding (STADELMAN 1913), were later described. Gastric varices were diagnosed at conventional roentgen examinations for the first time in a case with oesophageal varices (SCHIATSKI 1931). Since then several authors have published cases of gastric varices diagnosed by this method (TEMPLETON 1944, EVANS & DELANY 1953, EVANS 1959, WOHL & SHORE 1959, GUTCEMANN &

PARCHWITZ 1959) Gastric varices in these instances were usually associated with oesophageal varices. Gastric varices without demonstrable oesophageal varices have been diagnosed in several cases of prehepatic obstruction (SAMUEL 1948, BELGRAD *et coll* 1964, FLEMING & SEAMAN 1968). The former may however be mistaken for other lesions at conventional roentgen examinations (BRECKOFF & HERTZOG 1953, SMOONLER 1956) or be missed (ROSSI *et coll* 1967).

Gastric varices may produce three different roentgenographic appearances. External pressure from subserosal varices may cause tumour like bulging masses, usually located close to the cardia or smaller rounded filling defects with a diameter of 1 to 2 cm scattered throughout the fornix (EVANS & DELANY 1953). Tortuous impressions of moderate sized varices in the fornix give the mucosa a characteristic lobulated, bubble like appearance (SAMUEL 1948). An indirect sign of extensive gastric varices is thickening of the gastric wall, which causes downward displacement of the gastric gas in the erect position (HODGES 1950).

The mucosal folds of the fornix have been investigated by SWART (1968) in a series of cases that included normal conditions, gastritis, gastric and duodenal ulceration, carcinoma of the antrum as well as intrahepatic and prehepatic obstruction. Splenoportal phlebography was performed in cases of intra- and prehepatic obstruction, but the frequency of gastric collaterals was not reported. Only in one case with severe prehepatic obstruction were changes characteristic of gastric varices evident.

It has been stated that gastric varices should develop before oesophageal varices, because of the direct transmission of increased portal or splenic vein pressure to the gastric veins (KEGARIES 1934, TEMPLETON 1944, SAMUEL 1948). If oesophageal varices can be demonstrated, gastric varices almost certainly will also be present (KARR & WOHL 1960), they are easily overlooked even at autopsy, and their incidence must be higher than previously claimed (FELDMAN & FELDMAN 1956).

All cases in a splenoportographic series with portal hypertension had gastric collaterals that were large and numerous in a third of the cases (ROUSSELOT *et coll* 1956). However, collaterals are not invariably demonstrated by splenoportal phlebography in cases with gastrooesophageal varices and moderate portal hypertension (GREENE *et coll* 1965). This may be due to the effect of gravity on the contrast medium with unsuitable positioning of the patient or temporary changes in flow (EKMAN 1957).

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The aim of the present investigation was to analyze the reliability of the conventional roentgen examination of the stomach in cases with gastric varices,

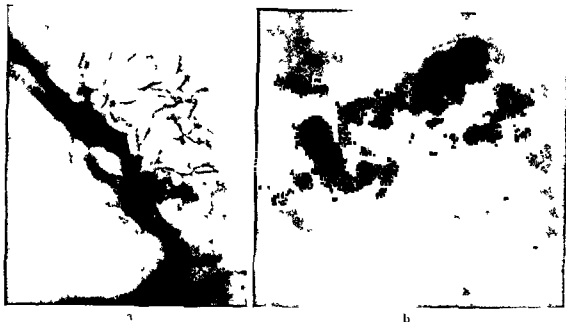


Fig 1 a) Lobulated bubble mucosal folds in the fornix of a case with splenic vein thrombosis  
b) Gastric collaterals corresponding in size and location to the mucosal distortion in (a) demonstrated by splenoportal phlebography

cirrhosis, 2 with splenic vein thrombosis and 1 case with portal vein thrombosis. The findings could not be differentiated from mucosal distortion of other origin without the help of splenoportal phlebography. A coarse but not 'bubble-like' appearance of the mucosa in the fornix was noted in 14 cases.

The thickness of the gastric wall was 20 mm or more in 9 cases of intrahepatic obstruction and in 1 case of portal vein thrombosis. According to HONGES (1950) downward displacement of the gastric gas in the erect position may be caused by (1) enlargement of the lesser lobe of the liver, (2) enlargement with upward and medial encroachment by the spleen, (3) interposition of fluid or pus between the stomach and diaphragm, (4) extensive thickening of the gastric wall with consequent encroachment upon the lumen of the stomach due to phlegmonous gastritis, massive varicosities within the gastric wall or a gastric tumour.

Separate enlargement of the lesser lobe of the liver is rare, and in the present investigation no hepatomegaly could be diagnosed by roentgen examination. Indeed, most cases had atrophic livers.

Splenomegaly was noted in 23 cases. Medial intrusion by the spleen sometimes caused an impression on the lateral wall of the fornix and proximal part of the body of the stomach. Co-existing subdiaphragmatic encroachment may have displaced the stomach downwards in some of these cases. However, no case of



Fig 2 a) Bulging masses cranial and caudal to the cardia in a case of hepatic cirrhosis b) Coils of collaterals at the cardia demonstrated by splenoportal phlebography to correspond to the bulging masses in (a)



Fig 3 a) Bulging mass at the cardia in a case of hepatic cirrhosis Lobulated mucosal folds in the fornix b) Huge coil of collaterals at the cardia evident at splenoportal phlebography

splenic vein thrombosis appeared to have this downward displacement of the stomach, although 7 out of 9 cases had splenomegaly. Extensive oesophageal varices were diagnosed by roentgen examination in 9 of 10 cases with downward displacement of the gastric gas. Thus, this sign occurred only in advanced cases with large anastomoses between gastric and oesophageal veins at the cardia.

Interposition of fluid is not likely to have influenced the results as the measurements were made in films exposed in the erect position.

Cases with a coarse mucosa occurred in the present investigation. This appearance does not however explain the downward displacement of the gastric gas, since such cases were included in the control group in which this sign was absent.

No tumour was diagnosed in the present investigation or discovered at operation.

### Conclusions

Conventional barium examination of the stomach supplemented with a double contrast technique is an unreliable method of diagnosing gastric varices. Only in 4 advanced cases with large oesophageal varices was it possible to observe the fairly characteristic roentgenographic appearances of gastric varices, in another 2 cases gastric varices were suggested.

The findings at splenoportal phlebography were compared with those at conventional roentgenography and an additional 6 cases were found to have large, tortuous gastric 'folds' that corresponded to coils of varices evident at splenoportal phlebography. The varices could not be diagnosed at conventional roentgen examination alone. Downward displacement of the gastric gas was present in 10 cases and all except one had extensive oesophageal varices. The displacement may sometimes have been caused by splenomegaly and the diagnostic value of this sign is not highly considered. Splenomegaly was the most common indirect sign of gastric varices and was noted in 23 out of 28 cases. Splenoportal phlebography is still the most reliable roentgenographic method of demonstrating gastric varices.

### Acknowledgement

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### SUMMARY

The diagnostic reliability of the conventional roentgen examination in demonstrating gastric varices was analyzed in a material of 28 cases and confirmed by splenoportal phlebography. The roentgenographic appearances were characteristic only in 4 advanced

cases with large oesophageal varices. Downward displacement of the gastric gas in 10 cases and splenomegaly in 23 cases appeared to be indirect signs of gastric varices.

## ZUSAMMENFASSUNG

Die diagnostische Zuverlässigkeit der konventionellen Röntgenuntersuchung zum Nachweis von Varicen des Magens wurde bei einem Material von 28 Fällen analysiert und durch splenoportale Phlebographie bestätigt. Die röntgenographischen Erscheinungsbilder waren nur in 4 fortgeschrittenen Fällen mit grossen Varicen des Oesophagus charakteristisch. Die Abwärtsverlagerung des Gases des Magens in 10 Fällen und Splenomegalie in 23 Fällen traten als indirekte Zeichen von Varicen des Magens hervor.

## RÉSUMÉ

L'auteur a étudié l'exactitude du diagnostic des varices gastriques par l'examen radiologique ordinaire sur une série de 28 cas confirmés par phlebographie splenoportale. Les images radiologiques n'étaient caractéristiques que dans 4 cas avancés présentant de grosses varices œsophagiennes. Le refoulement vers le bas de l'air gastrique dans 10 cas et la splénomégalie dans 23 cas paraissent être des signes indirects de varices gastriques.

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## CERVICAL PHANTOM FOR EVALUATION OF DIFFERENT METHODS OF ROENTGEN EXAMINATION OF THE LARYNX

by

ANDERS HEMMINGSSON

A proper cervical phantom is almost essential for comparing different methods of roentgenologic examination of the larynx including investigations of the influence of different tube potentials on the film exposed in the a p projection. A phantom for dosimetry is defined by the International Commission on Radiological Units and Measurements (ICRU Report 10d, 1962) as 'a volume of tissue-equivalent material either large enough to provide adequate scatter or constructed to resemble some special object, such as part of the human body, for the purpose of measuring a dose distribution'. HULTBERG *et coll.* (1959) define an anatomic phantom for dosimetry as 'a reproduction of some part of the human body conforming, on the whole, to the relevant member both in external shape and in radiophysical characteristics of different portions'.

The demands in comparative roentgen diagnostic investigations of the larynx are however greater. The phantom should then constitute a true anatomic

unchanged after fixation and embedding in the phantom. The radiophysical properties of the different components of the phantom should correspond closely to those of human tissues, both with respect to attenuation of roentgen radiation in the 50 to 200 kV range as well as to attenuation of gamma radiation from  $^{60}\text{Co}$ . Its soft tissue substitute should be in solid form and mechanically durable so that objects simulating changes in the larynx may be constructed of this material and introduced in the phantom, the substitute should be resistant to aging and storage at room temperature.

Cervical phantoms for dosimetry have been constructed by MAURER (1955), FRANKE (1957), STUHL & TOURNIER (1958), and others. Thoracic phantoms have been used in comparative roentgenologic diagnostic investigations by HARRIS et coll. (1956) and BERGSTROM (1969), among other authors. No anatomic cervical phantoms fulfilling the requirements given above appear to have been described previously.

*Theoretical considerations.* The attenuation of photon radiation in the range 20 keV to 1.5 MeV depends on photoelectric, Compton and coherent scattering processes. The phantom material should therefore resemble biologic tissue as regards these attenuating processes. Attenuation by pair formation could be neglected since this cannot occur below 1.02 MeV and is of importance only above 2 MeV for soft tissue (ATTIX & ROESCH 1968).

The linear attenuation coefficient for the Compton reactions is proportional to the electron density of the material but independent of the atomic number. The coefficients due to the photoelectric and coherent scattering effects are proportional to the electron density of the material but depend also on the atomic number. MAYNEORD (1937) gave a formula for the calculation of the effective atomic number for compounds taking into account the photoelectric effect. The formula (see below) contains an exponent  $s$ . Different values have been suggested for this exponent. It has thus been calculated to be 2.94 by WALTER (1927) — used by MAYNEORD (1937) and SPIERS (1946), among others — to 3.0 by MARKUS (1956) and 3.4 or higher by WEBER & VAN DEN BERGE (1969). According to EVANS (in ATTIX & ROESCH 1968) the exponent is slightly increasing with photon energy having a value of 3.02 at 100 keV and 3.5 at 1 MeV. The effective atomic number for soft tissue equivalent material changes by at most 8% when the exponent rises from 2.9 to 3.5. This difference is of importance only at low photon energies, below 30 keV, where the photoelectric effect dominates (ATTIX & ROESCH 1968).

The exponent of the atomic number for coherent scattering is about 1.7 according to WEBER & VAN DEN BERGE (1969). Coherent scattering is of some importance at low energies, but contributes at most about 10% to the total attenuation of monoenergetic radiation in soft tissue equivalent material (ATTIX

& ROESCH 1968) The attenuation is therefore in the first place dependent on the effective atomic number calculated from the exponent  $2.94 - 3.5$

The phantom material should consequently correspond to the effective atomic number calculated from the exponent  $2.94 - 3.5$ , the electron density and the mass density

The electron density  $n_0$  is obtained from the expression

$$n_0 = N_0 \sum_i p_i Z_i / A_i$$

where  $N$  is Avogadro's number,  $\rho$  the mass density,  $p_i$  the fraction by weight of element  $i$ ,  $Z_i$  the atomic number of the element  $i$ , and  $A_i$  the atomic weight of the element  $i$

Calculations of the effective atomic number  $Z$ , were made from the formula given by MAYNEORD (1937) as

$$Z^{2.94} = \sum_i a_i Z_i^{2.94}$$

where  $a = N \rho p_i Z_i / A_i$ ,  $n_0$ , i.e. the fractional electron content of the element  $Z_i$

The attenuation of photon radiation in different kinds of soft tissue varies very little (OMNELL 1957) Muscle has been chosen as an example of soft tissue because its radiophysical properties are well documented. Muscle tissue has a mass density of  $1.0 \text{ g/cm}^3$ , an effective atomic number of  $7.42$  (SPIERS 1946, MARKUS 1956) and an electron density of  $3.36 \times 10^{23} \text{ electrons/cm}^3$  (MARKUS 1956). The corresponding values for water are  $1.0 \text{ g/cm}^3$ ,  $7.42$  (SPIERS 1946, MARKUS 1956) and  $3.34 \times 10^{23}$  (MARKUS 1956, WEBER & VAN DEN BERGE 1969), i.e. there is full conformity between muscle and water except for the electron density, where the difference is less than one per cent. Water may therefore be used to advantage as the reference in tests of phantom materials that are to substitute soft tissue.

*Material and methods* The skeletal structure used in the cervical phantom was a 12 cm long preparation containing vertebrae C2—C7 from a 61-year old man. The mineral content of the skeleton was assessed roentgenologically as normal. The cervical spine was excised in its entirety, together with the surrounding muscle, ligaments and spinal cord, at autopsy. Fixation was performed for 20 days in glutaraldehyde 2.5 % buffered with 6 g/l calcium acetate. The preparation, the volume of which was approximately 0.3 litre, was thereafter treated in four changes, for 24 hours in each, of 1 litre Polyethyleneglycol A 1000 (Union Carbide Co., New York) at a temperature of  $50^\circ \text{C}$  in order to reduce its water content. Polyethyleneglycol A 1000 with the chemical formula  $\text{HOCH}_2(\text{CH}_2-\text{OCH}_2)_n\text{CH}_2\text{OH}$ , is a polymer of ethylene oxide, it can be mixed with water to about 70 % at  $20^\circ \text{C}$  and has a flash point of  $266^\circ \text{C}$ , a melting point of  $37$  to  $40^\circ \text{C}$  and a mass density of  $1.10 \text{ g/cm}^3$ .

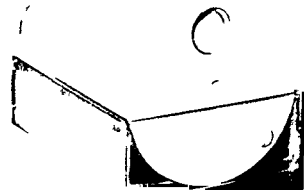


Fig 1 The phantom mounted in the plexiglass holder

MIX D (JONES & RAINE 1949), whose properties will be described below, was used as the substitute for soft tissue in the phantom. The cervical preparation was fused into this in four layers at a temperature of about  $140^{\circ}\text{C}$ , and a bore hole simulating the larynx and trachea, with a diameter of 25 mm, drilled in front of the preparation. The phantom was then turned on a lathe to form a cylinder with a diameter of 11.7 cm. The length of the phantom was 13 cm. It was then mounted in a plexiglass holder without a base.

The attenuation in the fixative used, glutaraldehyde, and in Polyethyleneglycol A 1000 was determined relative to water in a vessel with a 4 mm dividing wall and a base of plexiglass. The radiation passed through 9 cm layers of the substances to be compared. The polyethyleneglycol was in the solid form at a temperature of  $20^{\circ}\text{C}$ . Exposures were made with a Siemens roentgen tube, D200/30/50, with 1 mm Al inherent filtration and a 1.2 mm focal spot. The anode current was 20 mA and the tube potential 50, 100, 150 or 200 kV, with 2 mm extra brass filter at 200 kV, no extra filtration was applied at the lower potentials. The film, Cea Vicor X, emulsion number 035192, was exposed between Siemens rubra screens and developed at a temperature of  $36^{\circ}\text{C}$  in a 90 s processing unit. The same experiment was also conducted at 1.17 to 1.35 MeV, i.e. photon radiation from a 2 cm  $^{60}\text{Co}$  source, an industrial film 3M sigma, emulsion number R 9501-9, was used in a cassette with Siemens lead screens 0.10 and 0.15 mm thick, respectively. Developing was carried out in an 8 min processing unit at a temperature of  $35^{\circ}\text{C}$ .

The density of the films was measured with a Macbeth densitometer in 16 points for each of the two areas and the mean density calculated.

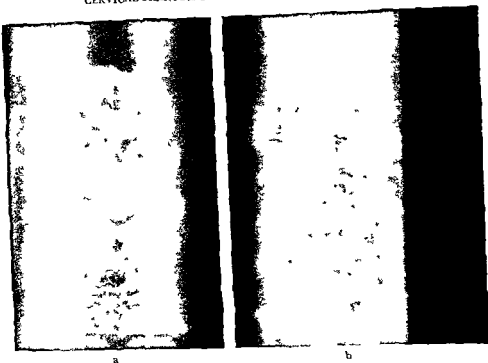


Fig 2 Roentgenogram of phantom a) a.p. and b) lateral projection

### Results

The complete phantom appears in Fig 1, with the drilled hole simulating the larynx and trachea in front, and the skeletal preparation, fused into the soft tissue substitute, as evident in the roentgenograms in Fig 2. No attempts were made to simulate the hypopharynx or oesophagus in the phantom as these structures do not interfere with the larynx in a.p. roentgenograms. Small gas-filled spaces were present in the phantom at the borderline between the embedded skeletal preparation and the phantom mass (Fig 2). These spaces were probably formed on fusion of the preparation in the Mix D.

The results of the densitometric determination for glutaraldehyde/water are given in Table 1. Neither in the 50 to 200 kV range nor at 1.17 to 1.33 MeV, i.e.  $^{60}\text{Co}$ , was there any significant difference in the film density.

The corresponding comparison between Polyethyleneglycol A 1000 and water indicated that the film density at 150 kV and at 200 kV + 2 mm extra brass filter, and at 1.17 to 1.33 MeV, i.e.  $^{60}\text{Co}$  photons, was 5 to 6 % lower for Poly

Table 1

*Film density for glutaraldehyde, Polyethyleneglycol A 1 000 and water at different tube potentials*

| Tube potential   | Film density     |                |                  |                            |
|------------------|------------------|----------------|------------------|----------------------------|
|                  | H <sub>2</sub> O | Glutaraldehyde | H <sub>2</sub> O | Polyethyleneglycol A 1 000 |
| 50 kV            | 1.78             | 1.78           | 1.45             | 1.47                       |
| 100 kV           | 1.58             | 1.62           | 1.41             | 1.40                       |
| 150 kV           | 1.46             | 1.47           | 1.56             | 1.48*                      |
| 200 kV           | 2.03             | 2.01           | 1.60             | 1.51*                      |
| <sup>60</sup> Co | 1.86             | 1.89           | 1.92             | 1.80*                      |

\* Significant difference at the 95 % level, the other measurements not significant at this level. The confidence interval is  $\pm 0.01$ – $0.02$ , except in the case of <sup>60</sup>Co, where it is approximately  $\pm 0.05$ , mostly due to inhomogeneity of the beam.

ethyleneglycol A 1 000 than for water (Table 1). No significant difference in the film density was evident at the lower tube potentials.

### Discussion

*Materials used as substitutes for soft tissue.* A large number of materials in solid form have been suggested as substitutes for soft tissue in radiologic investigations. Those which might have fulfilled the stated requirements for the present phantom are listed in Table 2 and Fig. 3, where their compositions and radiophysical properties are given. Information on the mass density and effective atomic number is lacking for the mixture of paraffin, boron oxide and magnesium carbonate (WEBER & VAN DEN BERGE 1969). It was not possible to prepare this material since no pressure chamber was available and its mass density has not been reported elsewhere.

Of the phantom materials listed in Table 2 and Fig. 3, 'pressed wood', paraffin and methylmethacrylate may be considered less suitable since they deviate too much from water as regards mass density, effective atomic number and electron density (HARRIS et al. 1956, MARKUS 1956). Colourless and blue cellophane have too high a mass density ( $1.3 \text{ g/cm}^3$ ) and electron density ( $4.14 \times 10^{23}$  and  $4.11 \times 10^{23}$  electrons/cm<sup>3</sup>, respectively) (MARKUS 1956), and Siemens Wax displays somewhat poorer correspondence with water than the others as regards

effective atomic number (690) (MARKUS 1956) Mixtures 1 and 2 are only obtainable in powder form (SPIERS 1943)

The remaining four phantom materials, Mix D (JONES & RAINE 1949, JENNINGS 1951, DAHL & VIKTERLOF 1958, 1960), M 3 (MARKUS 1956), silica-paraffin wax (HARRIS et coll 1956) and paraffin-boron oxide magnesium carbonate (WEBER & VAN DEN BERGE 1969), are approximately equivalent, with minor deviations from water as regards mass density, effective atomic number and electron density. Experimental investigations at 23 keV and 74 keV with the mixture of paraffin, boron oxide and magnesium carbonate have disclosed good agreement with water as regards attenuation (WEBER & VAN DEN BERGE 1969). The mixture must be processed in a pressure chamber, however, and the material is not stable for more than about a month and thus less suitable for the present phantom.

Silica paraffin wax and M 3 are resistant to aging, mechanically durable and easy to prepare and handle. A comparison between silica paraffin wax and water revealed a difference of about 8% in the density of the films at 30 and 50 kV, while this difference was somewhat smaller in the range 50 to 125 kV (HARRIS et coll 1956). No investigations at higher potentials appear to have been made. In view of the mass density of M 3, 1.06 g/cm<sup>3</sup>, an attenuation difference of about 6% compared with water would be expected (MARKUS 1956) although this does not appear to have been determined.

Several experimental investigations of the attenuation and scattering of ionizing radiation in Mix D and water have been conducted. JONES & RAINE (1949) reported a maximal difference of 2 and 3% determined as exposure, in transmitted and scattered radiation, respectively, after 5 cm Mix D and water for the radiation qualities 0.6 and 1.3 mm Al and 0.36 and 1.05 mm Cu HVL, i.e. within the range 50 to 250 kV (ICRU Report 10b, 1962). Similar results were obtained by JENNINGS, who reported that there was similarity between Mix D and water from 50 to 20 kV (1.93 to 0.145 mm Al HVL), while a small difference occurred at lower energies (JONES & RAINE). DAHL & VIKTERLOF (1958) recorded a six per cent difference in transmitted beam exposure behind 10 cm layers of Mix D and water at a radiation quality of 0.1 mm Cu HVL, corresponding to about 70 kV (ICRU Report 10b), while the difference was smaller at 0.8 and 1.6 mm Cu HVL, i.e. at approximately 160 and 250 kV (ICRU Report 10b). The same authors later reported that Mix D fulfilled attenuation requirements for dosimetry for <sup>60</sup>Co photons as well (DAHL & VIKTERLOF 1960). The effective atomic number of Mix D has been calculated experimentally by SPIERS to be 7.47 (JONES & RAINE). This substance is resistant to aging and storage, has good mechanical durability and can easily be shaped with power tools: it was therefore chosen as the substitute for soft tissue.



The gas-filled spaces at the borderline between the embedded skeletal preparation and the Mix D in the phantom constituted only a small proportion of its volume. They were therefore in the  $\alpha$  p films only visible lateral to the skeletal preparation and not in the region of the drilled hole simulating the larynx and trachea in the range 50 to 200 kV, or 1.17 to 1.33 MeV. They were therefore regarded as being of no practical significance.

By treatment of the skeletal preparation in Polyethyleneglycol A 1000, which does not vaporize appreciably at a temperature of 140° C, and by keeping the period of the temperature increase short, no change in the biologic tissue should have occurred.

### Conclusion

The cervical phantom described fulfils the requirements for comparative roentgenologic diagnostic investigations. Its skeletal part compared to living bone tissue was unchanged in anatomic properties and attenuation of ionizing radiation. Mix D as a substitute for soft tissue fulfils the requirements for equivalence with soft tissue in attenuation of roentgen quanta above 20 keV and for gamma radiation from  $^{60}\text{Co}$  and possesses the desirable physical properties. The locations and sizes of the different components of the phantom correspond with the regions they are intended to represent.

### Acknowledgement

The author takes this opportunity of thanking Ass. Prof. Bo Jung for his help in connection with the theoretic parts of the paper and for his generous support and advice.

### SUMMARY

An anatomic cervical phantom with radiophysical properties corresponding to biologic tissue in the 50 to 200 kV and 1.17 to 1.33 MeV ranges for roentgenologic diagnostic investigations is described. The materials employed are discussed in some detail.

### ZUSAMMENFASSUNG

Ein anatomisches Zervikalphantom für röntgendiagnostische Untersuchungen mit den radiophysischen Eigenschaften, die einem biologischen Gewebe im 50 bis 200 kV und 1.17 bis 1.33 MeV Bereich entsprechen, wird beschrieben. Das verwendete Material wird eingehender diskutiert.

## RÉSUMÉ

Description d'un fantôme anatomique cervical ayant les propriétés radiophysiques correspondant aux tissus biologiques pour les recherches de radiodiagnostic dans les domaines de 50 à 200 kV et de 1,17 à 1,33 MeV. L'auteur étudie en détail les matériaux employés.

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Abb 1 Patient mit Zyste in der rechten Niere a) Punktierte Zyste mit wasserlöslichem Kontrastmittel gefüllt b) Der grösste Teil des Kontrastmittels ist aspiriert und die Zyste ist mit 3 ml Pantopaque und Luft gefüllt c) Aufnahmen mit horizontalem Strahlengang mit Patienten in Bauchlage (c) und rechter Seitenlage (d)

Im hiesigen Institut haben wir seit mehreren Jahren die perkutane Nierenzystenpunktion in diagnostischer und therapeutischer Hinsicht angewandt. Anfangs benutzten wir die sogenannte Doppelkontrastmethode. Hierbei wurde die Zyste im Anschluss an die Punktion mit einem wasserlöslichen Kontrastmittel und Luft gefüllt, um die innere Kontur der Zyste deutlich darzustellen. Durch dieses Verfahren kann Malignität ausgeschlossen werden, und in diagnostischer Hinsicht ist diese Methode zufriedenstellend.

Da jedoch sowohl das wasserlösliche Kontrastmittel als auch die in der Zyste deponierte Luft allmählich resorbiert werden, ist es in vielen Fällen schwierig



Abb 2 a) Aufnahme mit vertikalem Strahlengang nach Zystenpunktion b) Aufnahme mit horizontalem Strahlengang welche die 3 Kontrastmittel (Luft, wasserlösliches Kontrastmittel und Pantopaque) übereinander demonstriert

die Zystengröße und damit die Behandlungsergebnisse nach einiger Zeit zu beurteilen. Wir führten deshalb 1963 die sogenannte Tripelkontrast- oder Pantopaque-Methode ein, über die ich bereits 1967 berichtet habe.

Bei dieser Methode werden in Anschluss an die perkutane Punktion mit Instillation eines wasserlöslichen Kontrastmittels und Luft 3 bis 6 ml Pantopaque in die Zyste injiziert. Pantopaque ist nicht resorbierbar und verbleibt in der Zyste. Damit ist die Beurteilung der Zystengröße und deren innerer Kontur bei Nachuntersuchungen erleichtert.

Ursprünglich wurde die Tripelkontrast- oder Pantopaque-Methode nur als rein diagnostisches Hilfsmittel benutzt. Bei den Nachuntersuchungen zeigte sich jedoch, dass Pantopaque zusätzlich eine therapeutische Wirkung hatte.

Inzwischen haben wir mit der perkutanen Zystenpunktion mehr Erfahrung gewonnen und die ursprüngliche Methode ist etwas modifiziert worden. In dieser Arbeit werden deshalb die zur Zeit angewandte Technik und ihre diagnostischen und therapeutischen Ergebnisse besprochen werden.

**Methodik:** Nach intravenöser Injektion von 20 bis 40 ml Iopaque 45 % wird der Patient auf einem Röntgentisch mit beweglicher Tischplatte und Bildverstärker in Bauchlage gelagert. Wie bei unserer Routine-Urographie wird Kompression angewandt. Nierenbecken, Nierenkelche und die vermutete Zyste sind dabei leicht zu erkennen.

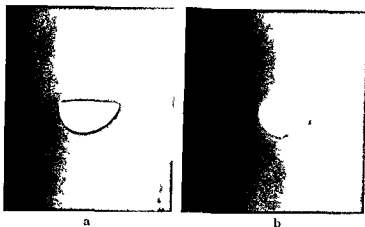


Abb 3 Gleicher Patient wie Abb 2. Aufnahmen mit horizontalem Strahlengang a) Nach 83 Tagen. Ein Flüssigkeitsspiegel zeigt, dass die Zyste sich nicht ganz zusammengezogen hat. b) Nach 6 Monaten ist der Flüssigkeitsspiegel verschwunden und die Zyste hat sich um das deponierte Pantopaque zusammengezogen.

Unter sterilen Bedingungen und in Lokalanästhesie wird eine dünne Nadel langsam und so senkrecht wie möglich in Richtung auf die Zyste hin eingeführt. Wir benutzen eine gewöhnliche Nadel für Spinalanästhesie, ungefähr 11 cm lang und mit einem äusseren Durchmesser von 0,9 bis 1,2 mm. Nachdem die Nadel die Rückenmuskulatur durchdrungen hat, wird der Patient gebeten, nicht zu atmen, und die Nadel wird in die Zyste eingestochen. Ein gutes Merkmal ist, dass sich die Nadel, solange sie sich noch in der Rückenmuskulatur befindet, nicht bewegt, aber mit der Respiration pendelt, sobald ihre Spitze in die Niere bzw. in die Zyste eingedrungen ist.

Nachdem die Nadel mit einem 50 cm langen Polyäthylenkatheter verbunden ist, werden je nach der Grösse der Zyste 10 bis 50 ml Zysteninhalt aspiriert und zu bakteriologischer und cytologischer Untersuchung gegeben. Dann wird eine entsprechende Menge Kontrastmittel (Isopaque 45 %) in die Zyste injiziert (Abb 1, 2). Der grösste Teil des Zysteninhaltes wird anschliessend entfernt, und die Zyste mit Luft und 3 bis 6 ml Pantopaque entsprechend ihrer Grösse gefüllt. Nach Entfernen der Nadel werden Röntgenaufnahmen in mehreren Projektionen mit horizontalem Strahlengang angefertigt. Die Anwendung des horizontalen Strahlenganges ist auch bei den späteren Kontrollen notwendig, um mit Sicherheit entscheiden zu können, ob die Zysten sich vollständig zusammengezogen haben (Abb 3).

Anfangs versuchten wir die Zystenflüssigkeit möglichst vollständig zu entfernen, bevor wir die Zyste mit Luft und Pantopaque füllten. Aber diese Be-

muhungen sind beschwerlich und nehmen lange Zeit in Anspruch. Aus diesem Grunde aspirieren wir jetzt nur das meiste des Zysteninhaltes, ohne Rücksicht auf einen Restinhalt zu nehmen. In Hinblick auf den Behandlungserfolg haben wir keinen Unterschied feststellen können.

Alle Schritte der Untersuchung. Die Punktion, die Aspiration der Zystenflüssigkeit und die Instillation des Kontrastmittels sowie der Luft werden mit Hilfe von Fernsehdurchleuchtung ausgeführt. Die bei Tageslicht ausgeführte perkutane Nierenzystenpunktion ist deshalb technisch einfach, erfordert keine Spezialinstrumente und bereitet dem Patienten wenig Beschwerden.

*Klinisches Material.* In den letzten 7 Jahren (1963 bis 1970) haben wir bei 44 Patienten mit einem expansiven Prozess in einer oder beiden Nieren die perkutane Nierenpunktion vorgenommen.

Zwei Patienten hatten ein Hypernephrom und ein Patient hatte ein chronisch entzündliches Infiltrat, einen sogenannten Pseudotumor (KING et coll. 1968, FELSON & MOSKOWITZ 1969). In allen 3 Fällen wurde die Diagnose durch Operation bestätigt.

Zwei Patienten hatten ein einseitiges polyzystisches Nierenleiden. Beide wurden später operiert. Im ersten Fall wurde eine Nephrektomie 4 Monate nach Zystenpunktion ausgeführt. Im zweiten Fall wurde 8 Tage nach der Zystenpunktion ein operativer Eingriff vorgenommen und die punktierte Zyste, die im linken unteren Nierenpol lokalisiert war, entfernt.

Drei Patienten hatten angeborene doppelseitige Nierenzysten. Ein operativer Eingriff wurde an diesen Patienten nicht vorgenommen.

Ein Patient hatte eine grosse retroperitoneale Zyste unbekannter Ätiologie im oberen linken Quadranten des Abdomens. Der Inhalt bestand aus gelber undurchsichtiger Flüssigkeit, und es handelte sich sehr wahrscheinlich um eine Pseudozyste des Pankreas. Ein operativer Eingriff ist in diesem Fall nicht vorgenommen worden. Die Zyste wurde in der üblichen Weise behandelt, indem 6 ml Pantopaque in dieselbe deponiert wurden. Das vorläufige Behandlungsergebnis ist zufriedenstellend gewesen, der transversale Durchmesser, der ursprünglich 17 cm betrug, war nach 10 Monaten auf 9 cm zurückgegangen.

Bei 37 Patienten wurde sowohl klinisch wie röntgenologisch das Vorliegen einer einfachen Nierenzyste vermutet. Die perkutane Nierenpunktion bekräftigte die Diagnose in 35 Fällen (94,6 %). In 2 Fällen kamen wir jedoch mit der Punktionsnadel in einen massiven Tumor, weshalb bei diesen ein operativer Eingriff vorgenommen wurde. In dem einen Fall handelte es sich um eine chronische Entzündung, einen sogenannten Pseudotumor, in dem anderen um ein Hypernephrom.

Das Hauptthema dieser Arbeit stellen die 35 Patienten, 14 Frauen und 21



Abb 4 a) Kontrastgefüllte Zyste nach Punktion b) Nach 15 Monaten. Die Zyste hat sich um das deponierte Pantopaque vollständig zusammengezogen

Manner, dar, die sämtlich einfache Nierenzysten hatten. Das Durchschnittsalter für diese Patienten war, als die Zystenpunktion ausgeführt wurde, 62,6 Jahre, der jüngste Patient war 25 Jahre alt, der älteste 79 Jahre. In den meisten Fällen wurde nur eine Zyste gefunden. Lediglich in zwei Fällen wurde die Punktion von 2 Zysten und in einem Fall von 3 Zysten vorgenommen.

In 6 Fällen waren die Zysten relativ klein und zentral in der Niere lokalisiert. Die übrigen gingen peripher vom Nierenparenchym aus. Obwohl diese peripheren oder subkapsularen Zysten die Tendenz haben, sich in die Umgebung der Nieren auszudehnen, verursachten sie in vielen Fällen eine erhebliche Kompression des Nierenparenchyms sowie Deformierung des Nierenbeckens und der Kelche.

Nur 6 der 35 Patienten mit einfachen Nierenzysten hatten Symptome, die auf dieses Leiden bezogen werden konnten, in den anderen 29 Fällen waren die Zysten asymptomatisch und wurden nur zufällig festgestellt.

Die aspirierte Zystenflüssigkeit war, von einem Fall abgesehen, klar. In diesem einen Fall ergab sich bei der röntgenologischen Untersuchung der expansive Prozess als eine einfache Zyste, aber die Flüssigkeit war getrübt und mit Blut vermischt, erfahrungsgemäss ein Zeichen für Malignität. Es handelte sich um eine 55-jährige Frau, die in den letzten zwei Monaten vor der Einlieferung periodisch starke Schmerzen im rechten Abdomen und massive Hamaturie

gehabt hatte. Kein Pantopaque wurde in die Zyste deponiert und die Patientin wurde sicherheitshalber nach 8 Tagen operiert. Der Operationsbefund zeigte eine einfache Zyste ohne Zeichen für Malignität.

Die restlichen 34 Patienten mit einfachen Nierenzysten wurden alle ausschliesslich durch Punktion in Verbindung mit Pantopaquedeponierung behandelt, ohne dass spätere operative Eingriffe vorgenommen wurden.

Die cytologische Untersuchung des Zysteninhaltes erwies sich in allen Fällen als negativ, und in keinem Fall konnten später klinische oder röntgenologische Anzeichen für Malignität gefunden werden.

Bei 24 der 34 Patienten haben sich die Zysten bis zu einem Durchmesser von unter 2 cm zusammengezogen, was dem Volumen der Kontrastmenge entspricht. Bei den restlichen 10 hat die Grösse der Zysten abgenommen.

Während den ersten Wochen und Monaten nach der Punktion wird das wasserlösliche Kontrastmittel und die Luft resorbiert, und die Zysten füllen sich wieder mit Zystenflüssigkeit. Nach 2 bis 3 Monaten hat sich der transversale Zystendiameter auf  $1/2$  bis  $2/3$  des Ausgangswertes verringert. Von diesem Zeitpunkt an verkleinerten sich die Zysten mehr und mehr. Bei den meisten Patienten haben sich die Zysten im Laufe von 9 bis 15 Monaten vollständig zusammengezogen (Abb. 4). In meiner früheren Arbeit (1967) berichtete ich über den ersten 20 Fälle. Diese Fälle wurden später weiter verfolgt. Die längste Beobachtungszeit betrug 86 Monate. In keinem dieser Fälle haben die Zysten später wieder an Grösse zugenommen.

In einigen Fällen haben sich die Zysten bereits nach 3 bis 6 Monaten vollständig zusammengezogen (Abb. 3), während es bei wenigen anderen bis zu mehreren Jahren in Anspruch genommen hat (Abb. 5).

Das deponierte Pantopaque verbleibt lange in den Zysten, aber auch dieses Kontrastmittel wird langsam resorbiert, und in wenigen Fällen war es nach mehreren Jahren verschwunden. In keinem Fall jedoch, in denen die Zysten sich schon ganz zusammengezogen hatten, haben sie später wieder an Grösse zugenommen (Abb. 6).

Keiner der 34 Patienten musste später operiert werden. Wiederholte Punktionen wurden in 3 Fällen (in 2 Fällen einmal und in einem Fall zweimal) notwendig. In einem von diesen war das Pantopaque aus der Zyste ausgetreten, wahrscheinlich verursacht durch einen zu grossen Durchmesser der Punktionsnadel. In den anderen zwei Fällen wurde bei der ersten Punktion zu wenig Pantopaque in den Zysten deponiert. Bei dem Versuch die Zysten vollständig zu entleeren wurde das bereits injizierte Pantopaque gleichzeitig entfernt. Nach erneuten Punktionen erschienen die Behandlungsergebnisse auch in diesen 3 Fällen zufriedenstellend.

Zystenpunktion mit Deponierung von Pantopaque wurde auch bei 2 Patien-





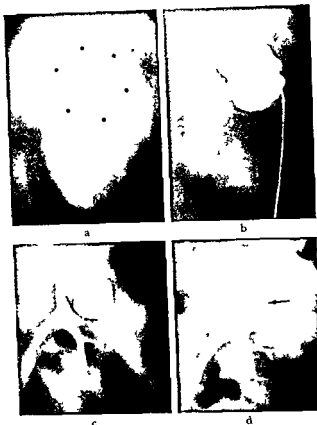
Abb 4 a) Kontrastgefüllte Zyste nach Punktion b) Nach 15 Monaten Die Zyste hat sich um die deponierte Pantopaque vollständig zusammengezogen

Männer, das, die sämtlich einfache Nierenzysten hatten. Das Durchschnittsalter für diese Patienten war, als die Zystenpunktion ausgeführt wurde, 62,6 Jahre, der jüngste Patient war 25 Jahre alt, der älteste 79 Jahre. In den meisten Fällen wurde nur eine Zyste gefunden. Lediglich in zwei Fällen wurde die Punktion von 2 Zysten und in einem Fall von 3 Zysten vorgenommen.

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Die aspirierte Zystenflüssigkeit war, von einem Fall abgesehen, klar. In diesem einen Fall ergab sich bei der röntgenologischen Untersuchung der expansive Prozess als eine einfache Zyste, aber die Flüssigkeit war getrübt und mit Blut vermischt, erfahrungsgemäss ein Zeichen für Malignität. Es handelte sich um eine 55-jährige Frau, die in den letzten zwei Monaten vor der Einlieferung periodisch starke Schmerzen im rechten Abdomen und massive Hamaturie



### Diskussion

Beim Hypernephrom handelt es sich in den meisten Fällen um einen gefassreichen Tumor, bei dem es heute dank der fortgeschrittenen Röntgentechnik möglich ist, die richtige Diagnose in etwa 95 % der Fälle zu stellen (EDHOLM & SELDINGER 1956, ÖDMAN 1956, FRIMAN-DAHL 1963, 1964, 1966, USON et coll 1963, WITTEN et coll 1963, PLAINE & HINMAN 1965, KAISER et coll 1967, EVANS 1968). Von den 37 Patienten in diesem Material, bei denen sowohl klinisch als auch röntgenologisch einfache Nierenzysten diagnostiziert wurden, zeigte die perkutane Nierenpunktion dass in zwei Fällen (5,7 %) ein massiver

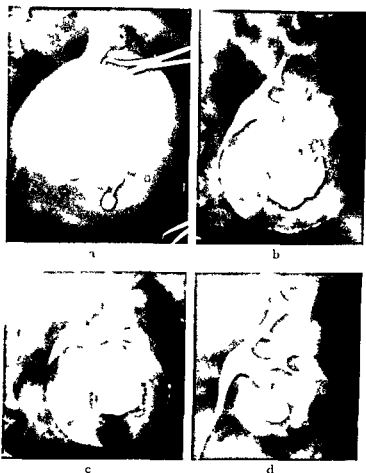


Abb 5 a) Zyste mit wasserlöslichem Kontrastmittel und Pantopaque gefüllt b) c) und d) Aufnahmen nach 3 6 und 24 Monaten Die Zyste hat sich kontinuierlich zusammengezogen In diesem Fall langsamer als gewöhnlich

ten mit einseitigen und 3 Patienten mit doppelseitigen Nierenzysten ausgeführt. Es handelte sich in allen Fällen um einzelne sehr grosse Zysten, die Kompression und Passagebehinderung am Übergang vom Nierenbecken zum Ureter verursachten. Diese Zysten haben in gleicher Weise auf Pantopaque wie die einfachen Nierenzysten reagiert. Da jedoch die Beobachtungszeit zu kurz und das Material zu klein ist, können die Behandlungsergebnisse noch nicht näher besprochen werden.

Wir haben in keinem Fall durch die Zystenpunktion irgendeine Komplikation gesehen, und die Nachuntersuchungen haben nicht gezeigt, dass das deponierte Pantopaque schädliche Wirkungen an den Nieren oder auf die Nierenfunktion gehabt hat.

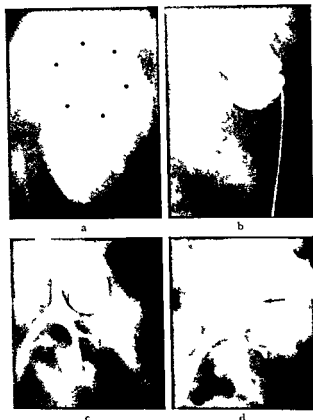


Abb 6 Linkseitige selektive Nephroangiographie Zentral  
gelegene Zyste b) Zystenpunktion c) Nach 12 Tagen Deut  
lich  
d)

### Diskussion

Beim Hypernephrom handelt es sich in den meisten Fällen um einen gefassreichen Tumor, bei dem es heute dank der fortgeschrittenen Röntgentechnik möglich ist, die richtige Diagnose in etwa 90 % der Fälle zu stellen (EDHOLM & SELDINGER 1956, ÖDMAN 1956, FRIMAN, DAHL 1963, 1964, 1966, USON et coll 1963, WITTEN et coll 1963, PLAINE & HINMAN 1965, KAISER et coll 1967, EVANS 1968). Von den 37 Patienten in diesem Material, bei denen sowohl klinisch als auch röntgenologisch einfache Nierenzysten diagnostiziert wurden, zeigte die perkutane Nierenpunktion, dass in zwei Fällen (5,7 %) ein massiver

Tumor vorlag. Der Operationsbefund ergab in einem der Fälle ein Hypernephrom (2,9 %).

Diese Untersuchungen bestätigen, dass in ganz wenigen Fällen ein Hypernephrom avaskular sein und mit einer einfachen Nierenzyste verwechselt werden kann. In diesen Fällen, wo der expansive Prozess entweder einen gefassarmen Tumor oder eine einfache Nierenzyste repräsentieren kann, wo aber das letztere am wahrscheinlichsten ist, sollte man eine perkutane Nierenpunktion ausführen. Für diagnostische Zwecke ist es nicht notwendig einen operativen Eingriff, der mit Morbidität und Mortalität belastet ist, auszuführen.

Gegen die perkutane Nierenpunktion werden ständig zwei Einwände hervorgehoben. Der erste ist, dass man durch die Punktion eines massiven Tumors Streuung von malignen Zellen bekommen kann. Aber dieses Risiko ist wahrscheinlich minimal (DEAN 1939, LINDBLOM 1946, 1952).

LINDBLOM vertritt unter anderem die Meinung, dass die Gefahr einer Streuung maligner Zellen bei einer Punktion aller Wahrscheinlichkeit nach geringer als bei einer Operation ist.

Die andere Einwendung ist, dass ein maligner Tumor zystisch degenerieren und dann mit einer einfachen Nierenzyste verwechselt werden kann. Wird jedoch die Zystenpunktion richtig ausgeführt, ist die Differentialdiagnose zwischen einer Degenerationzyste und einer einfachen Nierenzyste leicht. Degenerationszysten sind dickwandig und haben eine unregelmässige innere Oberfläche.

Einige Verfasser haben berichtet, dass sie bei operativer Behandlung von Nierenzysten gleichzeitig in derselben Niere carcinomatöse Veränderungen in 2,3 bis 7 % der Fälle gefunden haben (REHM et coll 1961, BRANNAN et coll 1962). In hämorrhagischen Zysten ist die Häufigkeit sogar bis zu 30 % angegeben worden (LOWSLEY & CURTIS 1945, LOWSLEY 1955). Es sind auch Fälle mitgeteilt worden, wo beide Leiden gleichzeitig vorkommen, und wo der Zysteneinhalt klar war (BRANNAN et coll 1962, KHORSAND 1965).

Sowohl einfache Nierenzysten als auch Hypernephrome sind keine seltenen Leiden, und es ist deswegen nicht unwahrscheinlich, dass in einigen Fällen beide Leiden gleichzeitig vorkommen. Wir haben niemals einen malignen Tumor von der Wand einer einfachen Nierenzyste ausgehen sehen. Wir stimmen deshalb vollkommen mit AINSWORTH & WEST (1951), EMMET et coll (1963) und SILVERMAN & KILHENNY (1969) überein, dass es sehr selten vorkommt, dass ein maligner Tumor von der Wand einer einfachen Nierenzyste ausgeht. Dieses muss man fast als eine Seltenheit betrachten.

Im Hinblick auf den therapeutischen Effekt von Zystenpunktionen sind die Ansichten geteilt. Einige Verfasser vertreten die Meinung, dass sogar grosse Zysten ganz verschwinden können (DEAN 1939, OLSSON 1962, DE WEERD



Abb 7 a) Angiographie Einfache Zyste der rechten Niere  
b) Zystenpunktion ohne Depomerung von Pantopaque  
c) Nach 39 5 Monaten Erneute Punktion mit Deponierung von 3 ml Pantopaque da die Zyste die Ausgangsgrosse wieder erreicht hatte Drei Monate später hatte sich die Zyste vollständig zusammengezogen d) Aufnahme nach 23 Monaten zeigt unverändert gutes Resultat

1962) Andere sind der Auffassung, dass der gute therapeutische Effekt nur vorübergehend ist Untersuchungen von WAHLQUIST & GRUMSTEDT (1966) bestätigen das letztere Bei 50 Patienten, die bis zu 19 Monaten nach der Punktion nachuntersucht wurden, fanden sie, dass die Zysten in 58 % der Fälle an Grösse abgenommen hatten Ihre späteren Nachuntersuchungen dagegen ergaben Verkleinerungen der Zysten nur in 35 % der Fälle

Unsere Erfahrungen stimmen vollständig mit den Beobachtungen von WAHLQUIST & GRUMSTEDT überein Ein Fall, der das bestätigt und der deutlich den therapeutischen Unterschied zwischen der früher angewandten Doppelkontrast

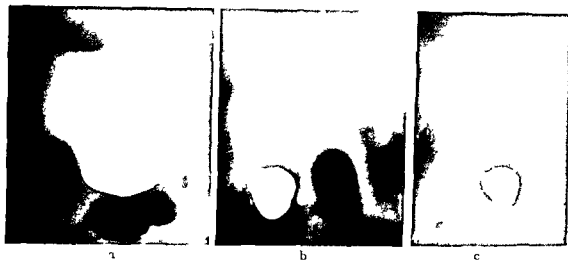


Abb 8 a) Zystenpunktion mit Deponierung von 5 ml Pantopaque ohne Aspiration von Zystenflüssigkeit Horizontaler Strahlengang b) Nach 3 Monaten Die Zyste ist fast vollständig zusammengezogen c) Nach 31 Monaten Die Zyste hat nicht wieder an Grösse zugenommen

methode und der jetzt verwendeten Tripelkontrastmethode zeigt, wird in Abb 7 illustriert. Es handelte sich um eine 22-jährige Patientin mit einer Zyste im rechten oberen Nierenpol. Im Jahre 1964 wurde eine gewöhnliche Zystenpunktion ohne Deponierung von Pantopaque vorgenommen, aber die Zyste füllte sich in kurzer Zeit wieder und erreichte 1967 die Ausgangsgrösse von 1964. Nach erneuter Zystenpunktion 1967, diesmal mit Deponierung von 3 ml Pantopaque, zog sich die Zyste im Laufe von 3 Monaten zusammen und hat nach einer Beobachtungszeit von 23 Monaten nicht wieder an Grösse zugenommen.

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Auf dem Internationalen Radiologenkongress in Tokyo 1969 berichteten LINDGREN & WESTBERG über ihre Erfahrungen bei der Behandlung von einfachen Nierenzysten mit  $^{32}\text{P}$  in Form von Wismutphosphat. Seit 1963 wurden 20 Zysten behandelt, von denen 11 eine Beobachtungszeit von mindestens 5 Jahren hatten. Die Zysten hatten sich auf 1 bis 2 cm in 12 Monaten zusammengezogen und waren seitdem unverändert.

Pantopaque ist ein ölhaltiges Kontrastmittel. Die Fremdkörperreaktion des Organismus auf ölhaltige Medikamente ist zu einem gewissen Grad von ihrem Gehalt an freien Fettsäuren abhängig. Während ein Öl mit einem hohen Gehalt

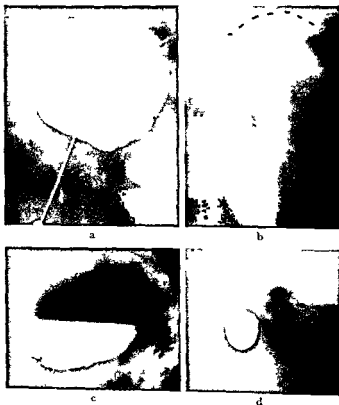


Abb 9 a) Zystenpunktion mit Deponierung von Pantopaque  
 b) Nach 8 Monaten Die Zyste hat aufgehört zu wachsen  
 erreicht kein Pantopa  
 c) Nach 16 Monaten  
 durch Punktion mit d  
 Nach 10 Monaten hatt  
 gen d) Aufnahme nach  
 tat (Horizontaler Strahlengang)

an freien Fettsäuren akute Gewebsnekrose verursacht, ruft ein Öl mit niedrigen Säurewerten nur einen leichten Grad von proliferativer Entzündung hervor

Sowohl klinische Untersuchungen als auch Sektionsbefunde haben gezeigt, dass Pantopaque, angewandt bei Myelographie, in einigen Fällen einen leichten Grad von Arachnoiditis bewirken kann (BERING 1950, JAEGER 1950, ERICKSON & VAN BAAREN 1953, SEHGAL et coll 1962, HURTEAN et coll 1963) Experimentelle Untersuchungen von HOWLAND & CURRY (1966) zeigten zusätzlich, dass die Injektion einer Mischung von Pantopaque und Blut zu erheblich stärkerer Gewebsreaktion führt, als die alleinige Injektion von Pantopaque



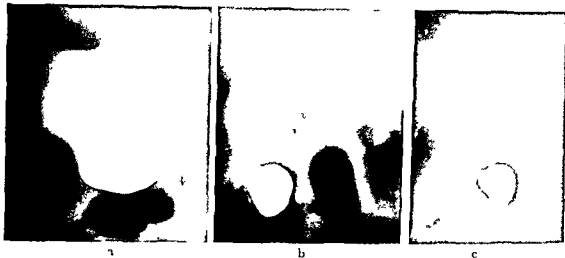


Abb 8 a) Zystenpunktion mit Deponierung von 5 ml Pantopaque ohne Aspiration von Zystenflüssigkeit. Horizontaler Strahlengang. b) Nach 3 Monaten. Die Zyste ist fast vollständig zusammengezogen. c) Nach 31 Monaten. Die Zyste hat nicht wieder an Grösse zugenommen.

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In einem der 2 Fälle mit einseitiger Zystenniere aus unserem Material wurde eine Nephrektomie 4 Monate nach der Zystenpunktion vorgenommen. Bei der histologischen Untersuchung war die Zystenwand, in welche das Pantopaque injiziert worden war, entzündlich verdickt. In den anderen Zysten, in die kein Pantopaque injiziert worden war, war die Wand dünn und mit flachem, nicht entzündlich verändertem Endothel bedeckt.

Es deuten deshalb sowohl unsere, wie die oben erwähnten Untersuchungen anderer Verfasser darauf hin, dass das deponierte Pantopaque die Ursache für das Zusammenziehen der Zysten ist. Aus diesem Grunde versuchen wir nicht mehr die Zysten vollständig von Flüssigkeit zu entleeren. Letzteres nimmt lange Zeit in Anspruch und kann beschwerlich sein. Jetzt aspirieren wir nur noch einen Teil des Zysteninhaltes, instillieren eine entsprechende Menge wasserlöslichen Kontrastes und Luft, um eine sichere Diagnose zu bekommen, und schliessen die Untersuchung durch Pantopaquedeposition in die Zyste ab.

Eine in dieser Weise ausgeführte Zystenpunktion nimmt erheblich weniger Zeit in Anspruch, während die Behandlungsergebnisse die gleichen bleiben. Ein Fall, der dieses zeigt, ist in Abb. 8 dargestellt. Es handelte sich um einen 79-jährigen Patienten mit einer Zyste im rechten unteren Nierenpol. Um eine sichere Diagnose zu erhalten, wurden zuerst 20 ml eines wasserlöslichen Kontrastmittels in die Zyste injiziert. Anschließend wurden nur 5 ml Pantopaque deponiert. Obwohl keine Zystenflüssigkeit aspiriert worden war, zog sich die Zyste in den nächsten 3 Monaten zusammen, und über eine Beobachtungszeit von 31 Monaten hat sie an Grösse nicht wieder zugenommen.

Anfangs verwandten wir Punktionsnadeln mit relativ grossem Durchmesser in der Absicht, eine möglichst grosse Öffnung in die Zystenwand zu stanzen. Wir hofften, dass diese Öffnung sich nicht wieder schliessen würde und, dass die reproduzierte Zystenflüssigkeit nach und nach in die Umgebung drainieren und dort resorbiert werden konnte. Diese Erwartungen erfüllten sich aber nicht. In einigen Fällen lief auch das deponierte Pantopaque aus den Zysten heraus, welche wieder an Grösse zunahmten und erneut punktiert werden mussten (Abb. 9). Wir verwenden deshalb jetzt möglichst dünne Punktionsnadeln, um das Herauslaufen des deponierten Pantopaques zu verhindern.

## ZUSAMMENFASSUNG

Die Differentialdiagnose zwischen einer Nierenzyste und einem Tumor ist auch mit Angiographie in etwa 4 bis 5 % der Fälle nicht möglich. In allen Fällen, in denen vermutet wird, dass eine Nierenzyste vorliegt, sollte aus diagnostischen Gründen punktiert werden. Im Anschluss an die perkutane Punktion hat der Verfasser 3 bis 6 ml Pantopaque in die Zyste deponiert. Bei 34 Patienten des Materiales haben dann alle Zysten sich ganz zusammengezogen oder an Grösse abgenommen. In keinem Fall war ein operativer Eingriff notwendig.

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## METHOD FOR ASSESSMENT OF FETAL WEIGHT

by

HANS G RINGERTZ

The number of techniques for assessment of fetal maturity is large, a fact that gives an indication of the difficulty of the problem. The presence of epiphyseal centres in the legs during the last weeks of pregnancy provides a valuable means of estimating fetal maturity while their absence is less significant (Bishop 1965). Measurements of a large number of linear parameters of the fetal body have further been used to estimate either the length, weight or gestational age. An integrated method worked out by FERNSTROM (1970) has been used at this hospital and makes use of several series of films with the fetus in different intrauterine rotations and known fetal weights. Thus, the roentgenogram in question may be fitted into its appropriate position in the series and hence the weight may be estimated. The method is successful when used by a skilled radiologist but there was a need for an easier method. A prerequisite was that only one roentgenogram should still be needed.

HOLMBERG & LILJEQUIST (1969) pointed out that the above mentioned measurements of linear parameters cannot be used for linear assessment of fetal weight or maturity. Regression equations where the sum of exponents for the linear parameters are 3 (e.g.  $\text{weight} = a^3$  or  $\text{weight} = b^x \times c$ ) ought to be used as the weight of a homogeneous body is a three-dimensional parameter. The most reliable and reproduceable linear parameter is probably the

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formulas were then used in 110 cases for a comparison with FERNSTROM's method (1970) mentioned above. These roentgenograms were used for an estimation of fetal weight with both methods and the result was compared with the actual birth weight. Finally the regression constants were calculated from the total 210 cases.

**Material** The first group of 100 roentgenograms and the second group of 110 films were selected with the following common restrictions: (1) no pathologic findings concerning the mother or the child had been recorded, (2) the delivery had occurred less than one week after the radiologic examination, and (3) the uterus did not contain more than one fetus.

The average and mode time between examination and delivery was 3.0 and 1.0 days, respectively.

The defining parameters of the whole material were

|                         | Mean     | Standard deviation |
|-------------------------|----------|--------------------|
| Birth weight            | 3.366 kg | 0.697 kg           |
| Lumbar vertebral length | 5.8 cm   | 0.5 cm             |
| Abdominal diameter      | 14.2 cm  | 1.5 cm             |

All parameters given were measured directly in the films without the application of any enlargement factor.

**Methods** One roentgenogram with the mother lying on the side and the beam in a vertical direction is taken. A compressor is used to reduce the depth of tissues to be penetrated (EDHOLM 1956, SCHREIBER & MORETTIN 1968). The focal distance is 1 m. The measurements of the lumbar vertebral length ( $V$ ) and the abdominal diameter ( $A$ ) are performed as indicated in Fig. 2.  $V$  lies between the middle point of the cranial surface of L1 and the middle point of the caudal surface of L5.  $A$  is obtained between the outer limits of the subcutaneous fat layers at the level of L1 and perpendicular to the spine.

The calculations of the multiple regression constants by least squares methods were computerized. The following regression equations were tested:

$$\text{Weight} = c_1 \times V^x \times A^{(3-x)} \quad (1)$$

$$\text{Weight} = c_2 \times V^x \times A^y \quad (2)$$

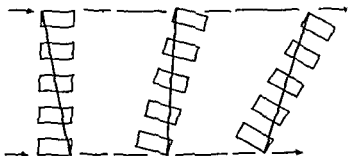
$$\text{Weight} = c_3 \times V + c_4 \times A + c_5 \quad (3)$$

where  $c$  were constants.

A comparison between the present method and FERNSTROM's method (1970) was performed in 110 cases. FERNSTROM made the estimations and both evaluations took place before the actual birth weight was known.



Fig 1 Roentgenogram of a fetal lumbar spine tilted  $0^\circ$ ,  $15^\circ$  and  $30^\circ$  respectively to the plane of the film. Practically no shortening exists when measuring between the upper contour of L1 and lower contour of L5; the schematic sideviews indicate that this is due to the fact that the actual measurement is a diagonal approximately parallel to the film when the spine is tilted  $15^\circ$ .



length of the lumbar spine (ZSEBOK 1957, FACERBERG & ROONEMA 1958, WEISHAAR & PORT 1964, MARGOLIS & VOSS 1968). One favourable feature of this measurement is evident in Fig 1. It is constant in length when obtained between the upper contour of the first lumbar vertebra (L1) and the lower contour of L5 even if the spine direction be inclined  $30^\circ$  to the plane of the film.

In order to correct the measured lumbar vertebral length for varying fetal nutritional conditions a second measure was introduced. Assuming an approximately circular abdominal transverse section the abdominal diameter of the fetus was measured at the level of L1 and perpendicular to the spine.

The aim of the present investigation was to present an easy method for assessment of fetal weight. This estimation should be based on one film and the calculations required should, if possible, involve correct dimensions. The basic parameters were taken to be the lumbar vertebral length ( $V$ ) and abdominal diameter ( $A$ ). Some different regression equations, including these two measurements and the observed birth weight, were tested in 100 cases. One of the

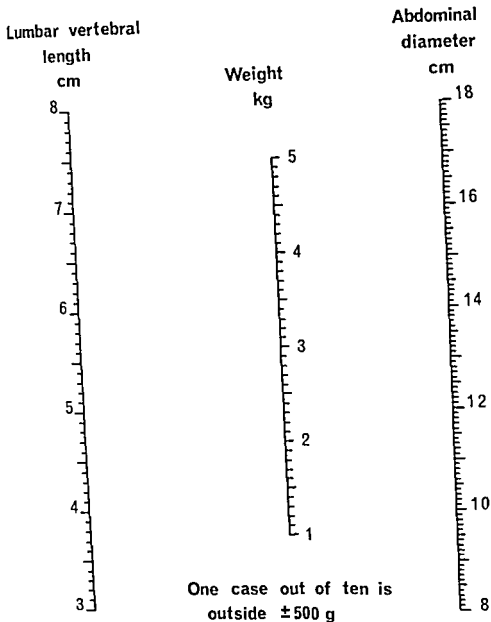


Fig 3 Chart for the assessment of fetal weight from the uncorrected measurement of the lumbar vertebral length and the abdominal diameter





Fig. 2. Roentgenogram of a fetus in the seventh gestational month with visible subcutaneous fat. The two measurements  $A$  and  $V$  have been indicated. The weight was estimated to be 1.6 kg.

The following linear equation was used for the comparison

$$\text{Birth weight} = c_6 \times \text{estimated weight} + c_7 \quad (4)$$

The ideal constant for  $c_6$  and  $c_7$  are 1.0 and 0, respectively

for the comparison with the FERNSTROM method. The new formula was a little superior in all respects and the differences mentioned were evenly distributed over the weight range.

The method could easily have been refined by introducing e.g. corrections for a non-circular abdominal transverse section but this was avoided because of the increased complexity in its use. The values  $V$  and  $A$  may also be used to assess the nutritional state of the fetus. For this purpose, the normal range ( $+2$  sigma) for the quotient  $A/V$  should be between 2.09 and 2.84. The significance of this quotient in e.g. diabetes and dysmaturity will be further investigated.

The present method of estimating fetal maturity has been applied for six months in some 100 cases and has been regarded as easy and a valuable complement to the information provided by examining the epiphyseal centres in a leg and the fetal subcutaneous fat.

## SUMMARY

A simple method of assessing fetal weight is presented. The fetal lumbar vertebral length and abdominal diameter are measured in a lateral roentgenogram and the weight is read directly from a chart. A range of  $\pm 0.5$  kg for the estimate covers the 90% probability. The quotient between the two measurements gives additional information about the nutritional state of the fetus.

## ZUSAMMENFASSUNG

Eine einfache Methode, das fetale Gewicht zu bestimmen, wird beschrieben. An lateralen Röntgenbildern werden die fetale Lumbalwirbellänge und der abdominale Durchmesser gemessen und das Gewicht direkt von einem Diagramm abgelesen. Ein Bereich von  $\pm 0,5$  kg dieser Bestimmung deckt die 90% ige Wahrscheinlichkeit. Der Quotient zwischen diesen beiden Messungen gibt zusätzliche Informationen über den Ernährungszustand des Fetus.

## RÉSUMÉ

Présentation d'une méthode simple pour déterminer le poids fœtal. On mesure sur une radiographie de profil la longueur de la colonne lombaire du fœtus et le diamètre abdominal. On lit le poids directement d'après une table. Une variation de plus ou moins 0,5 kg autour de cette estimation couvre une probabilité de 90%. Le quotient entre ces deux mesures donne des renseignements complémentaires sur l'état nutritionnel du fœtus.

## Results

Equation (1) was examined with different values for the exponent  $\lambda$  with the 100 'pilot cases'. The maximum for the correlation coefficient for  $\lambda$  was 1.1, which is close to the cylindric formula (2). The optimal constant  $c_0$  in formula (2) was calculated and the multiple correlation coefficient found to be 0.92. Practical considerations led to the testing of the less theoretically correct formula (3) for which the correlation coefficient was 0.93.

Using this formula the comparison with the FERNSTROM method (1970) gave the following results:

|                          | Fernstrom<br>method | Formula (3) |
|--------------------------|---------------------|-------------|
| Correlation coefficient  | 0.75                | 0.80        |
| Closest to correct value | 49 cases            | 61 cases    |
| Average deviation        | 0.322 kg            | 0.292 kg    |
| $c_0$ in formula (4)     | 0.79                | 0.89        |
| $c_7$ in formula (4)     | 0.853 kg            | 0.497 kg    |

The constants in formula (3) when calculated from the total of 210 cases had the following optimal values:  $c_3 = 0.484$ ,  $c_4 = 0.290$ , and  $c_5 = 3.549$ . These values refer to centimeters and kilograms and have been used to construct the chart in Fig. 3.

The standard deviation from regression when estimating the birth weight is 0.295 kg, meaning that  $\pm 0.5$  kg will involve a 90% probability. Thus one case out of twenty will have a weight of less than  $-0.5$  kg and one out of twenty more than  $+0.5$  kg with respect to the estimated value.

The quotient  $A/P$  was  $2.465 \pm 0.186$ . The quotient had no significant trend of dependence on the estimated birth weight.

## Discussion

The aim of the investigation as presented in the introduction could not be fulfilled in detail. It was evident that the theoretically correct formula (2) was acceptable, approximating the volume (weight) of the fetus as proportional to a cylinder of length  $P$  and diameter  $A$ . However, this formula had to be replaced with formula (3) for the following reason: an analysis of the distribution of the largest differences between calculated and observed birth weight disclosed that these were most frequent among the small and the large children. As these are the most interesting groups, the less correct formula (3) was used.

## CINEFLUOROGRAPHY IN DEMON- STRATING CALCIFICATIONS OF MITRAL VALVES

by

W MORTENSSON

The frequency of valve calcifications in mitral stenosis varies from series to series. EPSTEIN (1940), following autopsy of 148 consecutive patients with fatal rheumatic heart disease, reported calcifications in the mitral valves in 51 patients, all of whom had mitral stenosis, he did not, however, give the total number of patients with mitral stenosis. STEINER et coll (1954) observed valve calcifications in 53 per cent (25/48) of patients who had died from mitral disease. As for the frequency of valve calcifications present at operation BAILEY et coll (1957) gave 42 per cent, BADEN (1958) 39 per cent, MICHELL (1960) 32 per cent (men 46, women 28 per cent) and GUSTAFSON (1966) 36 per cent of patients.

Fluoroscopy, spot film roentgenography, body section roentgenography and cinefluorography have all been employed for demonstrating valve calcifications. GENOVESE (1951) and STEINER et coll (1954), who relied upon the first two methods sometimes supplemented by tomography, demonstrated calcifications in the valves in 23 and 21 per cent, respectively. LUKKO et coll (1958) described calcifications in the aortic or mitral valves in 24 of 48 patients. The results of the roentgen examination were not compared in these publications with those ob-

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Roentgen and operative findings could be compared in 83 patients, in 76 of whom the results agreed regarding the occurrence of the calcifications. Roentgen examination revealed calcifications in 2 patients, small in one and large in the other, that could not be palpated at operation, in 1 patient the surgeon felt a small calcification and in 3 patients diffuse calcifications, not demonstrable at preoperative roentgen examinations.

### Discussion

The degenerative changes in mitral valves develop over many years, and gross calcifications are not demonstrable until some twenty years after the acute stage of rheumatoid valvulitis. Even if severe fusion of the valves and shortening of the chordae occur without calcifications, high correlation between the presence of such calcifications on the one hand, and the severity of degenerative changes and impaired mobility of the valves on the other may exist. This was reflected in the present series, which indicated, first that calcifications in the valves were much more common in males and females with coexisting mitral insufficiency than in those without and secondly, that the stenosis, as judged from the descent of the anterior mitral valve, was more marked in patients with calcifications. The symptoms are therefore also more severe in patients with calcifications in the valves (Wynn 1933, Ellis et coll. 1964).

It is not known why calcifications in the valves occur so much more often in men than in women. In the present material the age distribution of the men was the same as that of the women, but of patients with calcifications, the men were somewhat younger than the women (median age of men with mitral valve calcifications 47 years, of women 50 years). The interval between the acute stage of valvulitis and the present investigation, where known, was on the average somewhat longer in men than in women. It is possible that the calcifications in the valves occur a little earlier in men than in women.

The differences in the published frequencies of calcifications in the valves may be explained by limitations of the examination methods used and any differences in composition of the series. Judging from what has been said, calcifications might be expected to be found more often at necropsy and at operation. The patients of the present series differed from one another in the degree and duration of the stenosis. Several patients had no symptoms or signs and the heart condition had been discovered incidentally at routine examination. The material is therefore less selected than a surgical or necropsy series, but subjects with mild or no symptoms or signs are obviously underrepresented.

The reliability of the method may be roughly assessed by comparing the roentgen and operative findings. Agreement between these findings was better in

tained by other examination methods. WYNN (1953) pointed out that at operation or necropsy of patients with mitral stenosis small calcifications not revealed by fluoroscopy were present. BADEN (1958), MICHELI (1960) and BJÖRK et coll (1963), who compared roentgen and operative findings, stressed that operation had disclosed small calcifications that had not been demonstrated at preoperative body-section roentgenography.

GUSTAFSON (1966), who used cinefluorography, detected calcifications in the mitral valves in 31 per cent of the patients, at operation of the same series calcifications were evident in 36 per cent. LITWAK et coll (1965) employed all available examination methods and considered cinefluorography to be better than any of the others. The technique for demonstrating calcifications in the valve with the aid of cinefluorography has been described by BARTLEY (1958) and JØRGENSEN (1961). The present paper concerns the frequency of valve calcifications in mitral stenosis in a series examined with cinefluorography as well as the reliability and the value of the method.

*Material and Methods* The clinical material consisted of 156 patients (61 men and 95 women) with mitral stenosis, about one third also had mitral insufficiency and several had aortic disease as well. Mitral stenosis was usually the main valve disease from the hemodynamic viewpoint. The patients' ages at the time of examination ranged from 20 to 64 years (median 47.5 years). The age distribution was the same for both sexes. The descent rate of the anterior mitral valve was determined by ultrasonic cardiography (EDLER 1955, EDLER et coll 1957, EFFERT 1959, GUSTAFSON 1966). Cinematography of the heart was performed with the patient in the lateral and right anterior oblique positions and with the aid of an image intensifier. Film rate 48 frames per second. Factors 90 kV, 130 to 160 mA, 3 to 6 ms. The films were examined in an Arnoe projector. The patients came from the department of cardiology and operations were performed at the department of thoracic surgery.

## Results

Calcifications in the mitral valves were demonstrated in 54 per cent of the men and in 15 per cent of the women, corresponding to 32 per cent of the entire series. The frequency of calcifications in patients with mitral stenosis alone was 38 per cent in the men and 9 per cent in the women, compared with 72 and 33 per cent, respectively, for those with associated insufficiency.

The descent rate of the anterior mitral valve was known in 26 patients with and in 50 of those without calcifications. It was above 15 mm/s in 19 per cent of the former and in 74 per cent of the latter.

## ZUSAMMENFASSUNG

Mit Hilfe der Cinefluorographie konnte in 54 Prozent von 61 Männern und in 15 Prozent von 95 Frauen die Mitralkstenose von wechselnder Dauer hatten, Verkalkungen festgestellt werden. Die Verkalkungen waren am häufigsten in den Fällen, in denen eine rheumatische Valvulitis eine ausgeprägte Stenose mit begleitender Insuffizienz hervorgerufen hatte. Die diagnostische Zuverlässigkeit der Methode ist hoch und sogar kleine Verkalkungen konnten entdeckt werden.

## RÉSUMÉ

L'examen cineradiographique de malades atteints de rétrécissement mitral de durée variable a permis de découvrir des calcifications chez 54 pour cent de 61 hommes et 15 pour cent de 95 femmes. Les lésions étaient beaucoup plus fréquentes dans les cas où la valvulite rhumatismale avait abouti à un rétrécissement marqué et dans les cas où les malades avaient aussi une insuffisance mitrale. Cette méthode est très fidèle au point de vue du diagnostic et permet de mettre en évidence même de petites calcifications.

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the present than in any series published. This is presumably because cinefluorography will demonstrate even small calcifications owing to their mobility, almost 15 per cent of the calcifications were 1 to 3 mm in diameter and thus not large enough to be demonstrated with ordinary roentgen diagnostic methods. No explanation can be offered for the disagreement in 7 patients between the roentgen and palpatory findings. The heart had not been opened in any of these patients and it is thus possible that the disagreement was due to difficulties in deciding by palpation whether a hard, fibrotic part contained calcifications. In the 2 patients in whom the preoperatively demonstrated calcifications could not be felt, their position and pattern of movement was such as to constitute clear evidence of their existence in the mitral valves. JORGENSEN (1963), who studied the possibility of demonstrating calcifications in the coronary vessels by cinefluorography and compared the findings with those made at necropsy, concluded 'unless the autopsy is done meticulously, more calcifications will be seen in the coronary arteries in the cineradiograms than will be detected and reported in the autopsy report'. This together with the fact that roentgenography had sometimes demonstrated even small calcifications in the valves, it is difficult to accept that large calcifications, felt in at least 3 patients, would not have been demonstrated at cinefluorography. One of these patients was examined twice.

Most authors assert that in the presence of calcifications the valves are usually changed to such an extent as to impair the prospects of surgical relief (WOOD 1954, BAHN et coll 1957, BADEN 1958, LILLIS et coll 1964). LITWAK et coll (1965) stated that closed valvulotomy never produced what they called 'satisfactory surgical relief regardless of the degree of calcification'.

Information before operation on the condition of the original valves is thus invaluable in the choice of the surgical method and contemplated insertion of artificial valves (TABER et coll 1963, GORI et coll 1969). Knowledge of the presence of calcifications also warns the operator of the risk of valve fracture and calciferous embolism, according to BADEN, thrombosis of the left atrium or auricular appendage seems to be more common in patients with gross calcifications.

The presence of calcifications in the mitral valves is a definite diagnostic sign of rheumatoid mitral stenosis.

## SUMMARY

Calcifications were present in 54 per cent of 51 men and 15 per cent of 95 women with mitral stenosis of varying duration examined by cinefluorography. The lesions were much more common where rheumatoid valvulitis had resulted in marked stenosis and where the patients also had mitral insufficiency. The diagnostic reliability of the method is high and even small calcifications will be demonstrated.

## ZUSAMMENFASSUNG

Mit Hilfe der Cinefluorographie konnte in 54 Prozent von 61 Männern und in 15 Prozent von 95 Frauen die Mitralstenose von wechselnder Dauer hatten Verkalkungen festgestellt werden. Die Verkalkungen waren am häufigsten in den Fällen, in denen eine rheumatische Valvulitis eine ausgeprägte Stenose mit begleitender Insuffizienz hervorgerufen hatte. Die diagnostische Zuverlässigkeit der Methode ist hoch und sogar kleine Verkalkungen konnten entdeckt werden.

## RÉSUMÉ

L'examen cineradiographique de malades atteints de rétrécissement mitral de durée variable a permis de découvrir des calcifications chez 54 pour cent de 61 hommes et 15 pour cent de 95 femmes. Les lésions étaient beaucoup plus fréquentes dans les cas où la valvulite rhumatismale avait abouti à un rétrécissement marqué et dans les cas où les malades avaient aussi une insuffisance mitrale. Cette méthode est très fidèle au point de vue du diagnostic et permet de mettre en évidence même de petites calcifications.

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## GASTRIC VARICES AND PHLEBECTASES

A gastrophotographic and roentgenographic investigation

by

NILS GABRIELSSON

The literature on gastric varices frequently contains inconclusive and in some respects contradictory data. If oesophageal varices can be demonstrated, gastric varices almost certainly will also be present (KARR & WOHL 1960). It has been stated that such varices should develop before oesophageal varices due to direct transmission of increased portal or splenic vein pressure to the gastric veins (KEGARIES 1934, TEMPLETON 1944, SAMUEL 1948). Evidence to support this reasonable statement has not been obtainable due to inadequate means of recognizing gastric varices, these are easily overlooked, even at autopsy, and their incidence must be higher than previously claimed (FELDMAN & FELDMAN 1956).

Conventional roentgen examination of the stomach is not a reliable diagnostic method of demonstrating gastric varices (SWART 1968, GABRIELSSON 1971). The varices may appear as a bulging mass usually located close to the cardia or small rounded filling defects with a diameter of 1 to 2 cm scattered throughout the fornix (SCHATSKE 1931, EVANS & DELAVI 1953). Tortuous impressions of

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wall (STAEMLER 1956) A phlebectasis does not possess marked mural changes and should be distinguished from a varix (STAEMLER 1956) Gastric veins are usually not evident at endoscopy except singularly when the stomach is maximally inflated, or when gastric atrophy is present (MORRISSEY et coll 1967, SCHINDLER 1950) Visible veins are otherwise phlebectases

A collateral is a vessel functioning as an anastomotic by pass The collateral may dilate due to the increased pressure and flow, and the latter may be reversed The terms collateral and varix are often used without distinction in the portal system However, gastric varices or phlebectases do not need to function as anastomotic by passes

*Anatomy* The description by BUTLER (1951) will be followed when not otherwise reported Three layers of veins exist in the stomach the subepithelial veins the submucosal plexus and the subserosal veins The capillaries of the mucosa drain into a subepithelial venous plexus without valves, located between the bases of the glands and the muscularis mucosae Small veins pierce the muscularis mucosae and form a larger submucosal plexus, the vessels of which have a muscular coating and valves (MAXIMOW & BLOOM 1957) Veins follow the arteries through the muscularis externa into the tunica serosa, where they unite to form large subserosal veins These are drained together with the perioesophageal veins into the left gastric vein on the lesser curvature, and into the short gastric veins or the gastroepiploic vein on the greater curvature In about half of the cases a separate large subserosal vein crosses the dome of the fornix and receives veins from the submucosal plexus (DOENYER et coll 1955)

Three layers of veins in the oesophagus connect with corresponding layers in the stomach The capillaries of the mucosa drain into a subepithelial venous plexus without valves Numerous short veins pierce the muscularis mucosae and drain into a larger submucosal venous plexus At, or just above, the cardia inconstant valves may occur in the submucosal veins which direct the blood towards the stomach Large veins arise at frequent intervals from the longitudinal submucosal veins perforate the muscularis externa and reach the outer surface of the oesophagus They unite to form the perioesophageal veins, which connect the left gastric vein to the azygos vein or the posterior bronchial veins via the paraesophageally located v comitantes nervi vagi

Venous anastomoses between the stomach and the oesophagus exist in all three layers In the subepithelial plexus of the oesophagus the polygonal meshwork is replaced at the lower end by a more longitudinal arrangement of veins that join the denser subepithelial plexus of the stomach at the cardia A large number of small connections between the portal and venous systems are thus formed

The veins increase in number but decrease in diameter in the submucosal

moderate varices in the fornix give the mucosa a lobulated, bubble like appearance (SAMUEL 1948).

Splenoportal phlebography is the most accurate roentgenographic method of diagnosing gastric varices, but a collateral circulation is not invariably demonstrable in cases with gastroesophageal varices and moderate portal hypertension (GREENE et coll 1965) The authors report higher diagnostic accuracy with endoscopy in these cases

Gastroscopy is seldom performed in cases with gastroesophageal varices, since it is considered a contraindication due to the risk of rupture (SCHINDLER 1950) Gastric varices resemble oesophageal varices and are tortuous, distended and bluish in colour (MOERSCH 1948), according to this author care has to be exercised in distinguishing them from gastric rugae, small or moderate sized varices have however a tendency to bisect rugae at an angle of about 45 degrees A drawing published of gastric varices depicted small, tortuous, bluish vessels that appeared to be located within or just below the mucosa and bore no resemblance to mucosal folds (SCHINDLER 1950) Nor do they resemble the considerably larger varices that might be demonstrated by conventional roentgen examination Gastric varices are said to be difficult to discern by endoscopy (PANKE et coll 1960) Large varices have been mistaken for a lymphoma (SMOOKLER 1956), leiomyoma (BELGRAD et coll 1964) or not seen at all (ROSSI et coll 1967)

Histologic examination of the stomach in 2 cases with bleeding gastroesophageal varices revealed dilated veins throughout the whole gastric wall (PHEMISTER & HUMPHREYS 1947) The submucosal veins close to the cardia were so large that they must have caused the mucosa to bulge Dilated gastric veins were observed at microscopy in cases with gastrointestinal haemorrhage, but other signs of portal hypertension were not evident (COTTIER 1953, FOGEL & FEJER 1955, POHL 1957) The dilated veins in these cases did not seem to function as anastomotic by-passes and were considered to be cavernous haemangiomas of the phlebectasy type Other authors have pointed out the importance of a congenital factor in the genesis of gastric varices (BRECKOFF & HERTZOG 1953) This might explain their presence in cases where they seem to be nonfunctional so far as an anastomotic by-pass is concerned (TAYLOR & EGBERT 1951)

It appears that gastric varices have not been investigated at any length by endoscopy The aim of the present work was to compare the findings obtained at gastrophotography, conventional roentgen examination of the stomach, and splenoportal phlebography in a series of cases with intrahepatic and prehepatic obstruction

*Definitions* The following definitions will be used A varix is a nonreversible dilated and tortuous vein with hyalinisation of the muscular element of the

veins but subepithelial or submucosal oesophageal varices do not always develop in these cases (STEINER et coll 1957). Before the dilation of the gastrooesophageal anastomoses, the increased pressure is mainly exerted upon the gastric veins. These veins are exposed to high pressure mediated through the connections to the left gastric and short gastric veins even after the anastomoses have become dilated (SWART 1968).

In stenosis or thrombosis of the splenic vein, collateral vessels may develop via the short gastric veins to the submucosal plexus of the fornix, which is drained via the left gastric vein back to the portal vein. Collateral vessels to the oesophageal veins may arise if this latter route be obstructed. The main gastric collateral is the left gastric vein to the oesophageal veins in portal vein thrombosis. Collateral vessels may also develop via the short gastric veins.

*Material* The series comprised 40 cases in which gastric varices or phlebectases were diagnosed or suggested at gastrophotography performed in a total of 600 cases between 1966 and 1969. Conventional roentgen examination of the stomach and oesophagus were performed not more than 14 days before gastrophotography in 25 out of 40 cases. In 7 cases over a month had passed between the two examinations but no treatment that could have influenced the appearances of the varices was given in the meantime. Splenoportal phlebography was performed in 10 cases and transcapillary portography in 8 other cases. Less than 14 days had passed between the gastrophotography and portography in 14 of 18 cases examined by both methods. There were 12 female and 28 male patients aged from 16 to 80 with an average of 46 years. The series could be divided into two groups according to the type of obstruction.

Prehepatic obstruction was diagnosed in 4 cases including 1 case of portal vein thrombosis and 3 cases of splenic vein thrombosis. Intrahepatic obstruction was suggested in 36 cases, among which hepatic cirrhosis was confirmed by biopsy in 19 cases and at operation in 2 cases. Hepatic metastases were believed to have caused intrahepatic obstruction in 2 cases of advanced malignancy. In one of these, the liver was enlarged and massively infiltrated at autopsy about 6 months afterwards. The remaining 13 cases of intrahepatic obstruction underwent no hepatic biopsy. In 6 of these cirrhosis was evident clinically and biopsy was not considered necessary for the diagnosis. Cirrhosis was clinically suggested in 6 other cases. One case was, for various reasons, not thoroughly investigated but chronic alcoholism made cirrhosis probable.

Gastrointestinal haemorrhage occurred before gastrophotography in 25 cases with intrahepatic and in 2 cases with prehepatic obstruction. Splenomegaly was diagnosed by roentgen examination in 19 cases with intrahepatic obstruction and in all 4 cases with prehepatic obstruction. Two additional cases had previously had splenomegaly, but splenectomy had been performed before the



plexus at the lower end of the oesophagus. They then become congregated in the four or five longitudinal mucosal folds, which begin a short distance above the cardia, the veins in these folds are markedly tortuous and connect the submucosal plexus of the oesophagus to that of the stomach and thus form an anastomosis between the portal and venous systems. In the last centimeters of the oesophagus the mucosa and the submucosa are firmly attached to the muscularis externa, so that oesophageal varices do not occur in this area (KEGARIES 1934).

The perioesophageal veins are directly connected to the left gastric vein through its oesophageal branches and thus form a third anastomosis between the portal and the venous systems. The paraesophageal veins are connected to the portal system only via the perioesophageal veins. Injection experiments have suggested that the perioesophageal connections provide an easier route than the anastomosis in the other two layers (BUTLER 1951). Contrast medium injected into the left gastric vein passed a slightly longer distance in the subepithelial than in the submucosal oesophageal plexus, in spite of the larger diameter of the latter vessels. This was probably due to the tortuosity of the submucosal veins normally present at the lower end of the oesophagus.

*Pathology.* Increased venous pressure due to congestion may cause dilated veins (STAEMLER 1956). With portal hypertension dilated veins have been noted in the omentum and the mesentery, as well as in the gastric, duodenal and abdominal walls (MCINDOE 1928, SCHOENMACKERS & VIETEN 1957, STEPHAN & MIETHING 1968). The submucosal veins of the stomach and intestine are particularly distended (MERKEL 1956), compared to the size of oesophageal varices the dilatation of these is much less. Histologic examinations reveal no marked mural changes, so they may be classified as phlebectases, they are said not to be evident macroscopically and are consequently not recognized at roentgen examinations or with endoscopy (STEPHAN & MIETHING 1968). However, the increased filling of blood in the gastric veins may be apparent indirectly at roentgen examinations as a coarsening of the mucosal folds (SWART 1968).

The hepatopetal flow decreases when the obstruction becomes more complete and gradually changes to a hepatofugal flow by way of collaterals. The left gastric vein is the main gastric collateral vessel in intrahepatic obstruction but the short gastric veins may also participate. Blood may be shunted to any of the three oesophageal layers after the dilatation of the anastomoses to the oesophagus. Communications between the gastric and retroperitoneal veins may develop and no oesophageal varices appear in these cases (DOEHRNER et coll 1956, FLEMING & SEAMAN 1968). Large collateral vessels may extend from the perioesophageal veins to the systemic circulation via the paraesophageal

Table 1

*Distribution according to results of gastrophotography, type of obstruction and confirmation of varices by operation or autopsy in 40 cases*

| Gastrophotographic findings     | No of cases | Type of obstruction |                 | Confirmation of varices by operation or autopsy |
|---------------------------------|-------------|---------------------|-----------------|---|
|                                 |             | Prehepatic          | Intrahepatic    |   |
| Coil of varices close to cardia | 2           | —                   | 2 <sup>1</sup>  | 2   |
| Moderate varices                | 13          | 3 <sup>1</sup>      | 10 <sup>2</sup> | 10  |
| Probable varices                | 4           | —                   | 4 <sup>3</sup>  | 1   |
| Isolated phlebectases           | 20          | 1                   | 19              | 4 <sup>3</sup>                                  |
| Probable phlebectases           | 1           | —                   | 1               | —   |
| Total                           | 40          | 4                   | 36              | 17  |

<sup>1</sup> Phlebectases suggested in 1 case

<sup>2</sup> Phlebectases diagnosed in 1 case

<sup>3</sup> Phlebectases diagnosed in 7 cases and suggested in 1 case

<sup>4</sup> Phlebectases diagnosed in 1 case and suggested in 2 cases

<sup>5</sup> In 2 cases the confirmed varices were located in the oesophagus and in the other 2 cases gastric varices but not phlebectases were confirmed

Table 2

*Distribution according to results of gastrophotography and roentgen examination of the stomach and oesophagus in 40 cases*

| Gastrophotographic findings     | No of cases | Roentgen examination of |               |                     |
|---------------------------------|-------------|-------------------------|---------------|---------------------|
|                                 |             | Stomach                 |               | Oesophagus          |
|                                 |             | Coarse mucosa           | Normal mucosa | Oesophageal varices |
| Coil of varices close to cardia | 2           | 2*                      | —             | 2                   |
| Moderate varices                | 13          | 10                      | 3             | 9                   |
| Probable varices                | 4           | 4                       | —             | 1                   |
| Isolated phlebectases           | 20          | 9                       | 11            | 4                   |
| Probable phlebectases           | 1           | 1                       | —             | —                   |
| Total                           | 40          | 26                      | 14            | 16                  |

\* In both cases a bulging mass was also demonstrated close to the cardia

## Results

The distribution of cases from the results of gastrophotography, type of obstruction and confirmation of varices is presented in Table 1. The distribution of cases according to the results of gastrophotography and roentgen examination

gastrophotography in order to establish a splenorenal shunt

*Technique* Roentgen examination of the stomach was performed as a routine with a standard technique without TV fluoroscopy. Moderate amounts of barium emulsion and compression were used for examining the mucosa. The patient was examined erect, prone and supine. Air swallowed during the barium meal was used for double contrast examinations in the supine position. If a mass were probable, gas-generating powder was given to distend the stomach completely. Roentgen examination of the oesophagus consisted of a standard technique including spot films in supine-oblique and erect oblique positions.

Splenoportal phlebography was performed by puncture of the spleen during TV fluoroscopy. A catheter (Pe 160) was threaded on a Pitkin lumbar needle and allowed to remain in the spleen after the needle had been withdrawn and about 50 to 70 ml of Urografin 60 % were injected through the catheter at a pressure of 1.4 to 1.6 kp by a Gidlund injector. The examinations were carried out both prone and supine to reduce the effect of gravity on the contrast medium. Transcapillary portography was performed in cases in which prehepatic obstruction was suggested or when puncture of the spleen was considered to entail a risk. A Mikaelsson catheter (Pe 205) was inserted in the coeliac artery and directed towards the splenic artery so that most of the 100 ml Urografin 60 % injected might reach the spleen. This examination was performed only in the supine position.

Gastrophotography was carried out with Olympus gastrocams, models 5, 5 A and with fibergastrosopes, models GTF and GFB. Model 5 was used in 20 cases, 5 A in 16 cases and GTF in 2 cases. Models 5 A and GTF were both employed in 1 case and models 5 A and GFB in 1 case. Four cases were examined twice and 2 cases three times for control purposes. The various models have been described by several authors (GABRIELSSON 1966, HARA et coll 1967, OSHIMA 1966 and 1967, WILLIAMS 1968). The technique used by the present author differs from the conventional method in that the position of the camera is carefully controlled by TV fluoroscopy (GIDLUND 1965, GABRIELSSON 1970). The camera was positioned according to a standard schedule, which was slightly modified by the information obtained from the roentgen examination. Special care was used to obtain close up views of the mucosa of the fornix. The cardia was examined by retroflexing the camera (YOSHITOSHI et coll 1963). This technique may cause some trauma to the the cardia with models 5 GTF and GFB and the mechanism for advancing the film may be disturbed with model 5. In order not to rupture possible varices, model 5 was retroflexed only occasionally and the fibergastrosopes not at all. Model 5 A was, however, always easily retroflexed without increasing discomfort to the patient. No complications in splenoportal phlebography or gastrophotography occurred.

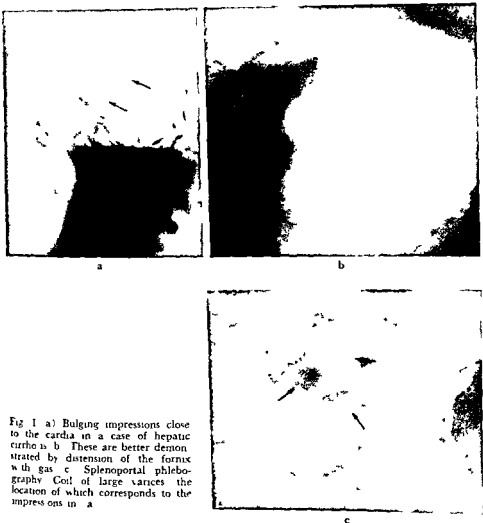


Fig 1 a) Bulging impressions close to the cardia in a case of hepatic cirrhosis b) These are better demonstrated by distension of the fornix with gas c) Splenoportal phlebography. Coil of large varices the location of which corresponds to the impressions in a

Roentgen examination of the stomach revealed a coarse mucosa in 14 of 17 cases with moderate or probable gastric varices. Rounded bulging impressions or lobulated mucosal folds were never evident. Examination of the oesophagus revealed or suggested varices in 10 of 17 cases. Splenoportal phlebography was performed in 6 and transcappillary portography in 5 cases with gastric varices of moderate size diagnosed by gastrophotography. Gastric collaterals were demonstrated in 10 cases, in 1 case a large collateral vessel had developed via the inferior mesenteric vein, but no gastric collaterals were evident.

Table 3

*Distribution according to results of gastrophotography and portography in 18 cases*

| Gastrophotographic findings     | No of cases | Portographic findings |        |                |
|---------------------------------|-------------|-----------------------|--------|----------------|
|                                 |             | Collaterals           |        | No collaterals |
|                                 |             | Gastric               | Others |                |
| Coil of varices close to cardia | 2           | 2                     | —      | —              |
| Moderate and probable varices   | 11          | 10                    | 1*     | —              |
| Isolated phlebectases           | 5           | 3**                   | —      | 2              |
| Total                           | 18          | 15                    | 1      | 2              |

\* 1 large collateral via the inferior mesenteric vein present

\*\* Retrograde filling of the short gastric and some slightly dilated gastric veins but no true collaterals evident in 1 case

of the stomach and oesophagus appears in Table 2. The distribution of cases from the results of gastrophotography and portography is evident in Table 3.

Large gastric varices close to the cardia were present in 2 cases with intrahepatic obstruction (Figs 1, 2). Gastrophotography revealed a coil of finger wide bulging varices without a bluish tinge. They could be distinguished from gastric folds because of their different orientation and tortuous course. Roentgen examination in both cases revealed a tumour-like, lobulated mass, the location of which was consistent with the varices observed by gastrophotography. Portography also demonstrated a large coil of varices close to the cardia and a huge collateral flow through the left gastric vein in both cases. Operation confirmed enormous gastric varices. Histologic confirmation of the location of the varices within the wall was not however obtained.

Gastric varices of moderate size were present at gastrophotography in 13 cases and were probable in 4 cases. These appeared as transverse, tortuous, slightly bulging impressions between the rugae of the fornix when in 5 cases the stomach was well inflated. They could be followed across several longitudinal folds as distinguished from transverse folds, which usually extend only from one longitudinal fold to the other. In the remaining 8 cases the varices appeared as rounded impressions 1 to 2 cm in diameter usually situated in the superior or anterior wall of the fornix. They caused slight bulging of the mucosa, usually between the gastric rugae. No blue tinge appeared through the mucosa in these varices of moderate size.



Fig 3 Splenoportal phlebography in early cirrhosis. Retrograde filling of the short gastric veins ( $\rightarrow$ ) and some slightly dilated tortuous gastric veins ( $\curvearrowright$ ). These are drained through the left gastric vein to the portal vein. The gastric veins do not function as collaterals even if dilated and tortuous.

veins were present in 2 cases. Retrograde filling of the short gastric and solitary slightly dilated gastric veins in one case could not be accepted as evidence of a true collateral circulation (Fig 3). No collaterals were demonstrated in the remaining 2 cases but in one of them the splenic vein was tortuous and dilated and the rate of flow decreased.

*Differential diagnosis.* Deeply located gastric varices may suggest malignancy if they are large enough to cause bulging of the mucosa; a coil of large varices close to the cardia may be diagnosed as carcinoma both by roentgen examination and endoscopy. Deep impressions near to the cardia may also be caused by intussusception of oesophageal mucosa, an enlarged left lobe of the liver, enlarged lymph nodes (WOHL & SHORE 1959), a tumour of the tail of the pancreas or a lipoma outside the stomach (unpublished observations by the author). Tortuous varix impressions have been diagnosed as a lymphoma (SMOOKLER 1956) and rounded varix impressions as a leiomyoma (BELGRAD *et coll.* 1964) at endoscopy. Varices of moderate size causing rounded impressions may be mistaken for sessile polyps. Varices are usually flatter and more longitudinal than the latter. However, the main diagnostic problem is to distinguish varices of moderate size from gastric rugae. All cases except 3 of the present material with demonstrated or probable large or moderate varices had coarse mucosal folds, probably due to venous congestion (SWART 1968). The varices in a coarse oedematous tunica mucosa have to reach a considerable size before they can be distinguished by endoscopy.

Phlebotomies are easily distinguished at gastrophotography from submucosal vessels, which are evident in gastric atrophy through the thin and transparent

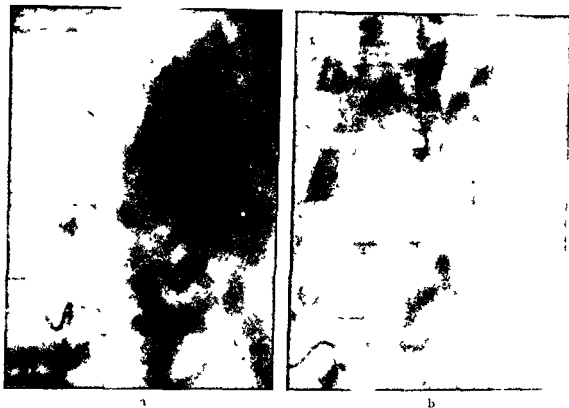


Fig 2 a) Transcapillary portography. Coil of large varices b) Slow rate of circulation in the varices permits better demonstration later in the series

Small superficial phlebectases were present or suggested in the fornix at gastrophotography in 13 cases with obvious or probable larger gastric varices. The phlebectases appeared as bluish, tortuous distended vessels with a diameter of about 3 mm, they could be followed across several longitudinal folds and were orientated towards the cardia and sometimes passed through it into the oesophagus. The vessels seemed to rise slightly above the surface of the mucosa and probably were dilated submucosal veins without mural changes, and were consequently classified as phlebectases. Isolated phlebectases without demonstrable varices were diagnosed by gastrophotography in 20 cases and suggested in 1 case.

Roentgen examination of the stomach revealed coarse mucosal folds in 10 of these and normal findings in the remaining 11 cases. Oesophageal varices were present at conventional roentgen examination in 4 cases with isolated phlebectases in the fornix. Splenoportal phlebography was performed in 3 cases with isolated phlebectases and transcapillary portography was carried out in another 2 of these cases. Collateral vessels of moderate size to dilated gastric



Fig 4

Fig 4 Bulging tortuous gastric varices in the dorsal wall of the fornix Same case as in fig 1

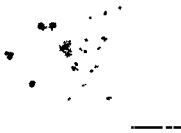


Fig 5

Fig 5 Coil of large varices just cranial to the cardia Same case as in fig 2



Fig 6

Fig 6 Small phlebotomases orientated towards the cardia and crossing the mucosal folds of the dorsal wall of the fornix



Fig 7

Fig 7 Tortuous phlebotomases crossing the main direction of the mucosal folds of the greater curvature of the fornix Same case as in fig 3



Fig 8

Fig 8 Tortuous phlebotomasis on the greater curvature of the fornix



Fig 9

Fig 9 Submucosal branching vessels not to be confused with phlebotomases



mucosa The slight yellow to greenish colour of the atrophic mucosa and the netlike appearance caused by submucosal vessels, which are not tortuous, preclude diagnostic errors Phlebectases must not be confused with veins occasionally evident at the fornix when the stomach is fully inflated (MORRISSEY et coll 1967) The author has observed such veins in about 10 cases without evidence of portal hypertension or gastric atrophy These vessels were usually not tortuous or orientated towards the cardia as they are with phlebectases Differentiation was occasionally difficult and the diagnosis of phlebectases then had to be supported by clinical data before it could be accepted Small gastric rugae in oblique light must not be interpreted as veins The phlebectases should be reproduced in several photographs taken at different angles to establish a firm diagnosis

### Discussion

No case with known oesophageal varices was examined earlier than fourteen days after massive bleeding, and haemorrhage was never induced by gastrophotography Large oesophageal varices were ruptured by trauma due to a gastrocamera in case not included in the present investigation The patient would not cooperate and closed his jaws on the connecting tube while vomiting No films were exposed and the bleeding fortunately stopped With reasonable cooperation the risk of varix rupture seems to be minimal

The entire fornix and cardia must be examined properly to ensure the diagnosis of gastric varices and phlebectases by endoscopy The stomach has to be distended with air to stretch out the rugae It is possible that the increased intraluminal pressure slightly compresses the varices and phlebectases, and it has been suggested that the stomach should be only partially inflated in these cases (MOERSCH 1948) However, the present author has found it necessary to distend the stomach completely because this appears to be the only possible way to distinguish varices and phlebectases among the gastric rugae

Deeply located, large gastric varices may cause bulging of the tunica mucosa This is usually apparent in all three methods: roentgen examination, portography and gastrophotography Varices may in moderate cases cause only slight bulging which may still allow a diagnosis by gastrophotography but be difficult to establish by conventional roentgen examination, the appearances are caused by large subserosal varices (EVANS & DELANY 1953) Firm support from the surroundings is required to produce bulging through the muscularis externa of the gastric wall, without this support the varices should expand towards the surroundings The necessary support outside the stomach can only be achieved in certain anatomic sites where it is obtained by the diaphragm, spleen and

Table 4

*Clinical data in 29 cases with hepatic cirrhosis and gastric varices or phlebectases demonstrated by gastrophotography*

| Gastrophotographic findings | No of cases | Ascites | More than 3 spider naevi | Bilirubinemia | BSP > 15 % cases examined |
|-----------------------------|-------------|---------|--------------------------|---------------|---------------------------|
| Gastric varices             | 12          | 8       | 8                        | 8             | 7/7                       |
| Phlebectases                | 17          | 1       | 4                        | 5             | 7/12                      |

left lobe of the liver. These locations seem to be most common with bulging gastric varices (SAMUEL 1948, BRECKHOFF & HERTZOG 1953, EVANS & DELANY 1953, SMOOKLER 1956). When subserosal varices do not bulge, they can be diagnosed only by portography. This occurred in 2 cases in the present investigation in which gastrophotography revealed phlebectases but no subserosal varices.

The clinical data in Table 4 indicate that an advanced stage of disease present in 12 cases with hepatic cirrhosis and varices was revealed by gastrophotography. The portal pressure exceeded 30 cm of water in 6 of 7 cases examined at operation. The gastrophotographic diagnosis of varices in these 12 cases was of clinical value only in 1 case without demonstrable oesophageal varices and 3 cases with visible active bleeding from gastric varices.

Phlebectases are discerned only if the resolving power of the gastroscope or gastrocamera is high. It was difficult to discern them in the congested oedematous mucosa of advanced hepatic cirrhosis, although in these cases large subserosal varices may more easily be defined. All cases with gastric varices probably also had phlebectases although they were not evident in 7 cases and only suggested in 2 cases. Conventional roentgen examination and portography cannot diagnose phlebectases because of their small size. Gastric collateral vessels demonstrated in cases with phlebectases are probably due to contrast filling of co-existing varices. The location of phlebectases within the gastric wall could not be established in the present investigation as resection of the stomach was never performed and the phlebectases were overlooked at the autopsy of several cases. Histologic examination of the stomach was unfortunately not performed. However, at the autopsy of a case, not included in this investigation, with advanced hepatic cirrhosis and reported as bleeding from large oesophageal varices the author found typical phlebectases in the fornix. Histology revealed dilated submucosal veins with an estimated diameter of 3 to 4 mm. No marked changes in the wall of the veins were evident.



The submucosal veins of the oesophagus reach a considerably larger size than the submucosal gastric veins with portal hypertension and gastrooesophageal collaterals although the intraluminal pressure should be about the same (STEPHAN & MIEHNING 1968). The probable explanation of this phenomenon is that the connective tissue in the tunica submucosa of the stomach is firmly attached to the muscularis externa and the veins have a muscular coating.

Bleeding from gastric varices arises from co-existing submucosal phlebeectases or still smaller subepithelial veins (PHEMISTER & HUMPHREYS 1947). The author has observed that haemorrhage from gastric varices may cause protracted slow bleeding suggesting anemia. Direct haemorrhage from subserosal gastric varices may occur if these large veins traverse and disrupt the muscularis externa, this has been reported (SMOOKLER 1956).

### Conclusions

Gastric varices were diagnosed by conventional roentgen examination only in a few advanced cases in which large tortuous subserosal varices caused a bulging mass. Slight distortion of the mucosal folds caused by varices of moderate size failed to be distinguished from that of other origin by conventional roentgen examination. Phlebeectases could not be diagnosed by this method.

Splenoportal phlebography or transcappillary portography enables the demonstration of large and moderate sized varices provided they function as anastomotic by-passes. Phlebeectases are too small to be discerned by portography and probably do not function as by-passes.

Gastrophotography reveals varices of moderate size provided they cause some bulging of the tunica mucosa. Phlebeectases may be diagnosed by gastrophotography. In fact, endoscopy is the only method available to diagnose phlebeectases which represent a valuable indirect sign of portal hypertension. They may be revealed in cases in which portography and conventional roentgen examination of the stomach and oesophagus fail to demonstrate varices.

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### SUMMARY

Forty cases of pre- or intrahepatic obstruction have been investigated with gastrophotography and conventional roentgen examination. In 18 cases gastric varices were diagnosed by conventional roentgen examination.

Table 5

*Comparison of diagnostic accuracy in 18 cases examined by all three methods*

| Demonstrated findings           | Gastrophotography | Conventional roentgen examination | Portography |
|---------------------------------|-------------------|-----------------------------------|-------------|
| Coil of varices close to cardia | 2                 | 2                                 | 2           |
| Varices of moderate size        | 11                | —                                 | 10          |
| Phlebectases                    | 5                 | —                                 | —*          |
| Total                           | 18                | 2                                 | 12          |

\* Portography demonstrated gastric collaterals in 2 cases with phlebectases but gastric varices were however not demonstrated by gastrophotography

The clinical data in Table 4 suggest that a less advanced stage of cirrhosis was usually present in cases with isolated phlebectases than in those with larger subserosal varices. There was sometimes no clinical probability of hepatic cirrhosis until phlebectases were demonstrated by gastrophotography, early cirrhosis was afterwards confirmed by biopsy or supported by laboratory tests. The presence of gastric phlebectases is a valuable early indirect sign of portal hypertension, these may be demonstrated by gastrophotography at an earlier stage than oesophageal or subserosal gastric varices may be revealed by conventional roentgen examinations or phlebography. There are strong reasons to believe that phlebectases in the fornix develop before true gastric collaterals and oesophageal varices. Oesophageal veins with a diameter above 1 mm are considered as varices (DOFFNER et coll 1956). Small oesophageal varices are easily overlooked at conventional roentgen examination and difficult to distinguish from mucosal folds at endoscopy (CONN et coll 1967). Oesophagoscopy was not performed in any case with isolated gastric phlebectases in the present investigation and, even if it had been, co-existing small oesophageal varices could not have been excluded. The statement that gastric varices develop before oesophageal varices could therefore not be absolutely confirmed. However, it is highly probable that gastric phlebectases are produced by the increased pressure exerted on gastric veins before true collaterals are formed, at this stage the phlebectases have no function as an anastomotic by-pass. In one case of the present investigation with isolated phlebectases at gastrophotography, splenoportal phlebography was performed before gastric collaterals had developed. Retrograde flow of contrast medium through the short gastric veins was demonstrated and some slightly dilated gastric veins were filled although no true anastomotic by-pass appeared (Fig 3).

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fornix in 29 cases, revealed only by gastrophotography, represent a valuable indirect sign of portal hypertension and probably occur before collaterals to the stomach and oesophagus develop

## ZUSAMMENFASSUNG

Vierzig Fälle mit prä oder intrahepatischer Obstruktion wurden gastrophotographisch und mit konventioneller Röntgenuntersuchung des Magens studiert. Portographie wurde in 18 Fällen vorgenommen. Durch Gastrophotographie wurden in 15 Fällen Varizen des Magens nachgewiesen, durch konventionelle Röntgenuntersuchung in 2 Fällen und durch Portographie in 14 Fällen. Venenerweiterungen im Fornix bei 29 Fällen, die nur durch Gastrophotographie nachzuweisen waren, bilden ein brauchbares indirektes Zeichen eines portalen Hochdrucks und entwickeln sich wahrscheinlich bevor die Kollateralen des Magens und Ösophagus auftreten.

## RÉSUMÉ

Quarante cas d'obstruction pré ou intra hépatique ont été examinés par gastrophotographie et par examen radiologique habituel de l'estomac. Une portographie a été faite dans 18 cas. Des varices gastriques ont été mises en évidence par gastrophotographie dans 15 cas, par examen radiologique habituel dans 2 cas et par portographie dans 14 cas. Les ectasies veineuses de la grosse tubérosité dans 29 cas, se révèlent uniquement par la gastrophotographie, sont un signe indirect précieux d'hypertension portale et apparaissent probablement avant que ne se développent les collatérales dirigées vers l'estomac et l'oesophage.

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## HYDROSTATIC SIALOGRAPHY AS AN INDEX OF SALIVARY GLAND DISEASE IN SJÖGREN'S SYNDROME

by

D M CHISHOLM, G S BLAIR, P S LOW and K WHALEY

Sjogren's syndrome is a chronic benign disorder affecting middle aged females and is characterized by the triad by xerostomia, keratoconjunctivitis sicca and a connective tissue disease, usually rheumatoid arthritis and less commonly systemic lupus erythematosus, progressive systemic sclerosis, polymyositis or polyarteritis nodosa (BLOCH et coll 1965). In order to qualify for the diagnosis of Sjogren's syndrome two of the three main components must be present. The term sicca syndrome is used to describe the association of xerostomia and keratoconjunctivitis sicca in the absence of a connective tissue disorder (BLOCH et coll 1965).

Keratoconjunctivitis sicca and rheumatoid arthritis are diagnoses readily made according to well defined criteria. However, the position is less clear with regard to the salivary gland component of the symptom complex. Sialography and salivary flow rate investigations have both been used to assess the severity of salivary gland disease in patients with Sjogren's syndrome (BLOCH et coll 1965,

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Fig 1 Normal 15 lateral-oblique sialogram



Fig 2 Punctate sialectasis



Fig 3 Globular sialectasis

MAYNARD 1965, MASON et coll 1967, BERTRAM 1967, ERICSON 1968) In addition, in view of the strong autoimmune association of Sjogren's syndrome, focal lymphocytic sialadenitis of the minor glands (CHISHOLM & MASON 1968), and the presence of the salivary duct auto-antibody (BERTRAM & HALBERG 1964, BERTRAM 1967, MACSWEEN et coll 1967) have been used to detect salivary gland involvement in Sjogren's syndrome The use of scanning of the salivary glands using intravenous  $^{99}\text{Tc}^{\text{m}}$ -pertechnetate promises to be a further useful investigative procedure (HARDEN et coll 1968) The aims of this paper are to evaluate hydrostatic sialography and parotid flow rates in patients with Sjogren's syndrome with and without rheumatoid arthritis, and using these techniques attempt to provide an index of salivary gland dysfunction

### Materials and Methods

The criteria of BROCH et coll (1965) were used to diagnose Sjogren's syndrome Rheumatoid arthritis was diagnosed using the criteria of the American Rheumatism Association (ROPES et coll 1958) and keratoconjunctivitis sicca by the technique of WILLIAMSON et coll (1967)

Sixty-four patients with Sjogren's syndrome were included in this investigation Twenty-one had the sicca syndrome and 43 had Sjogren's syndrome associated with rheumatoid arthritis Nineteen of the patients with sicca syndrome were females and two were males, whereas 38 of the patients with rheumatoid arthritis and Sjogren's syndrome were females and 5 were males All but 2 patients in each group had both parotid glands examined so that 124 parotid glands were included in the series A control series of 45 subjects without salivary gland or connective tissue disease were also examined by salivary flow rate measurement and bilateral hydrostatic sialography

*Oral and flow rate examinations* A careful history was taken from each patient of the presence, nature and duration of xerostomia, and of salivary gland enlargement and associated oral and pharyngeal symptoms of Sjogren's syndrome (BROCH et coll 1965) Parotid salivary flow examinations were carried out using a modified Carlson Crittenden cup (CARLSON & CRITTENDEN 1910) having an internal chamber diameter of 10 mm, an external chamber diameter of 20 mm and a depth of 4 mm The inner chamber was placed over the parotid duct orifice and the cup maintained in position by an air suction applied through the outer chamber Parotid saliva was collected under conditions of lemon juice stimulation following the method of MASON et coll (1967)

*Sialography* A standard hydrostatic technique (PARK & MASON 1966) was employed using Hypaque contrast medium A tapered polythene catheter was

Table

*Sialographic appearances and salivary flow results in 64 patients with Sjogren's syndrome*

|   | Normal    | Sialectasis |          |          | Atrophy  | Main duct dilatation |
|---|-----------|-------------|----------|----------|----------|----------------------|
|   |           | Punctate    | Globular | Cavitory |          |                      |
| Total number of parotid glands examined                 | 45        | 29          | 15       | 15       | 14       | 6                    |
| Number with sicca syndrome                              | 8         | 10          | 5        | 11       | 4        | 2                    |
| Sex distribution  | 8 ♀ 0 ♂   | 10 ♀ 0 ♂    | 3 ♀ 2 ♂  | 11 ♀ 0 ♂ | 4 ♀ 0 ♂  | 2 ♀ 0 ♂              |
| Number with Sjogren's syndrome and rheumatoid arthritis | 37        | 19          | 10       | 4        | 10       | 4                    |
| Sex distribution  | 29 ♀ 9 ♂  | 17 ♀ 2 ♂    | 10 ♀ 0 ♂ | 4 ♀ 0 ♂  | 10 ♀ 0 ♂ | 4 ♀ 0 ♂              |
| Mean parotid flow rate (lemon juice) ml/min             | 0.85      | 0.38        | 0.34     | 0.13     | 0.25     | 0.32                 |
| SE  | 0.07      | 0.04        | 0.06     | 0.04     | 0.05     | 0.07                 |
| Range   | 0.26—2.00 | 0.0—0.8     | 0.0—1.0  | 0.0—42   | 0.01—0.5 | 0.08—0.48            |

were modified by BLOCH *et coll* (1965) to punctate, punctate with immediate duct involvement, globular, and cavitory or destructive. In addition to these findings, atrophy of the duct system has been mentioned by ERICSON (1968). In this investigation we recognize three degrees of sialectasis, punctate, globular and cavitory, where the diameter of the sialectatic defects are  $< 1$  mm, 1—2 mm and  $> 2$  mm, respectively. Atrophy was defined as sparsity of duct branches and diminution in their calibre. Where it occurred main duct dilatation was noted. To ensure accurate assessment of sialectasis, templates showing the degrees of sialectasis and atrophy were superimposed on the films being examined. Examples of normal and abnormal sialograms are shown in Figs 1 to 5.

### Results

The distribution of sialographic abnormality is shown in the Table. In the disease group, 45 salivary glands were normal, 8 (20%) with sicca syndrome, 37 (44%) with Sjogren's syndrome complicated by rheumatoid arthritis, and 59 had sialectasis, of which 29 were punctate, 15 globular and 15 cavitory. Fourteen glands had atrophy of the duct system and a further 6 dilatation of



Fig 4 Cavitory sialiectasis and main duct dilatation



Fig 5 Atrophy of complete duct system (31 year old female)

inserted into the orifice of Stenson's duct and the contrast medium allowed to enter from a glass reservoir, positioned 70 cm above the patient's head. By this method, underfilling seldom occurs because the film is taken whilst the contrast medium is still flowing and the pressure, therefore, maintained. Overfilling rarely occurs because an almost constant pressure is employed in each case. Films were taken in the a.p. and lateral oblique position at the completion of the filling phase. A secretory film was taken five minutes after the completion of the filling phase. In order to standardize the test further, and to ensure rapid expulsion of the contrast medium, salivary flow was stimulated with a few drops of lemon juice, immediately following the filling phase film.

*Criteria of sialographic abnormality* BLATT *et coll* (1964) recognized four types of sialiectasis: punctate, globular, cavitory and destructive. These criteria

### Discussion

The aim of this investigation was to assess whether or not the apparent degree of parotid gland abnormality as noted on sialographic examination using a hydrostatic technique correlated with diminution of parotid gland function as assessed by the capacity of the gland to secrete saliva in response to lemon juice stimulation. It has been shown that patients with Sjögren's syndrome who have sialographic abnormalities have lower parotid rates than those patients with Sjögren's syndrome with normal sialographic findings. The mean parotid flow rate decreases with increasing degrees of sialectasis and extremely low flow rates were recorded in patients with cavitory sialectasis. However, it is interesting that patients with globular sialectasis do not have a significantly lower parotid flow rate than those with punctate sialectasis although the value is slightly lower. This suggests that the degree of parotid gland damage is probably of equal severity in patients having punctate or globular sialectasis.

Atrophy of the duct system detected by sialography in patients with Sjögren's syndrome is associated with considerable gland dysfunction as shown by the reduced mean flow rate which is significantly lower than that observed when punctate sialectasis is present ( $p < 0.05$ ). This finding is not altogether unexpected as ERICSON (1968) has shown that patients with duct atrophy on sialographic examination had severe histologic changes on parotid gland biopsy. Although the number of patients exhibiting dilatation of the main duct in the absence of any other abnormality is small, it is of considerable interest that the mean parotid flow rate was 0.32 ml/min. This is significantly lower than the mean flow rate in patients with Sjögren's syndrome having normal sialographic findings ( $p < 0.005$ ). This suggests that in the absence of sialographic evidence of damage to salivary duct epithelium, a significant decrease in function may have occurred and is supported by the further evidence obtained from the control series.

MAYNARD (1965) correlated sialographic abnormality with salivary flow rates in 73 patients with recurrent parotid swelling of whom 7 had Sjögren's syndrome. He noted that sialectasis alone or sialectasis associated with minor duct changes was associated with normal flow rates, whilst sialectasis with main duct changes and main duct changes alone was associated with reduced flow rates. BLATT *et al.* (1956) and ERICSON (1968) have suggested that changes in the main duct are probably the result of infection secondary to diminished flow rate. It would, therefore, appear logical to expect a higher incidence of main duct dilatation associated with salivary glands showing severe grades of sialectasis. In this series, 6 of 51 glands (11.8%) without evidence of sialectasis or atrophy had main duct dilatation whereas 2 of 29 (6.9%) with punctate sialectasis, 5 of 15 (33.3%) with globular sialectasis and 8 of 15 (53.3%)

the main duct without evidence of sialectasis or atrophy. Mean parotid salivary flow rates after lemon juice stimulation are also shown in the Table. The mean flow rate of the glands in patients with Sjogren's syndrome with normal sialographic findings was 0.85 ml/min (SE 0.07 ml/min) whereas the glands with punctate sialectasis the mean flow rate was 0.38 ml/min (SE 0.04 ml/min). This difference is highly significant ( $p < 0.0005$ ). The mean flow rate for the glands with globular sialectasis was slightly lower than those with punctate sialectasis (0.34 ml/min, SE 0.06 ml/min). The salivary glands exhibiting cavitory sialectasis had a mean flow rate of 0.13 ml/min (SE 0.004 ml/min). This difference is highly significantly lower than the mean value obtained in those glands with globular sialectasis ( $p < 0.0005$ ). The fourteen salivary glands with atrophy on sialographic examination had a mean flow rate of 0.25 ml/min (SE 0.05 ml/min). When compared to the mean flow rates of those glands with a normal sialographic appearance, the difference was noted to be highly significant ( $p < 0.0005$ ). The mean flow rate is also significantly lower than the mean flow rate noted in the glands with punctate sialectasis ( $p < 0.05$ ). However, no significant difference was noted between the mean flow rates of glands with atrophy or globular sialectasis. It can be seen from the Table that the mean flow rate found in glands with cavitory sialectasis was markedly lower than those with atrophic changes ( $p < 0.05$ ). It is interesting to note that the mean flow rate of the patients with dilatation of the main duct without sialectasis or atrophy was 0.32 ml/min (SE 0.07 ml/min). This is lower than the mean flow rate noted in patients with punctate or globular sialectasis but not significantly so. It is difficult to interpret this finding but it should be noted that whereas relatively large numbers of glands were included in the other groups, only 6 were in the group with main duct dilatation. The mean flow rate in this group is significantly lower, however, than in the group with normal sialographic findings, ( $p < 0.005$ ) and it is significantly greater than the flow rate noted in the group with cavitory sialectasis ( $p < 0.01$ ). Further we have examined each of these groups with sialectasis in order to assess whether duct dilatation or retention of contrast medium following the secretory phase was associated with a greater reduction in salivary flow rate than those glands not showing these changes. However, the numbers were small and could not be subjected to statistical analysis, but it is interesting to note that there was a tendency for flow rates to be slightly lower where duct dilatation or retention was observed, in addition to the predominant sialographic abnormality. The mean flow rate in 45 controls was 1.29 ml/min (SE 0.12 ml/min) which is significantly higher ( $p < 0.0025$ ) than the mean flow rate in patients with Sjogren's syndrome with normal sialographic findings (mean = 0.85 ml/min, SE 0.07 ml/min).

sungen nach Stimulation untersucht. Die Ergebnisse weisen darauf hin, dass die letztere Methode einen empfindlicheren Index für Dysfunktion der Parotis bildet.

## RÉSUMÉ

Les auteurs ont déterminé par sialographie hydrostatique et par mesures de débit stimulé le degré d'atteinte de la glande parotidienne chez des malades atteints de syndrome de Sjögren avec ou sans rhumatisme articulaire. Les résultats montrent que la deuxième méthode donne une mesure plus sensible du dysfonctionnement parotidien.

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with cavitory sialectasis had main duct dilatation as an associated feature. With the exception of the group of patients with punctate sialectasis the incidence of main duct dilatation increased with more severe grades of sialectasis. However, on statistical analysis using the chi-squared test (with a Yate's correction for small numbers) only in the glands with cavitory sialectasis was the prevalence of main duct dilatation significantly higher than those without evidence with sialectasis or atrophy ( $\chi^2 = 11.9841$ ,  $p < 0.001$ ). The prevalence of main duct dilatation in the group with cavitory sialectasis is not significantly different from the group with globular sialectasis. These findings support the view that main duct dilatation is associated with diminution in salivary flow rates in patients with Sjogren's syndrome. Main duct dilatation may follow infection and in this respect it is of interest that main duct dilatation is a feature of patients with recurrent chronic obstructive parotitis (MAYNARD 1965).

### Conclusions

It would appear from these results that in patients with Sjogren's syndrome the severity of sialographic abnormality is to some extent paralleled by decrease in parotid gland function as shown by lemon juice stimulated parotid salivary flow rates. However, this is by no means constant, as some patients with main duct changes occurring in the absence of sialectasis have a lower parotid salivary flow rate than patients with punctate or globular sialectasis. It would also be reasonable to conclude that the varying degrees of salivary gland destruction between patients having punctate or globular sialectasis are not marked as there is little difference between the mean parotid salivary flow rates of these two groups. These data support the view that salivary flow rates provide a more sensitive index of salivary gland disease than sialography and has been confirmed by the observation that patients with Sjogren's syndrome with normal sialographic findings have significantly lower parotid flow rates than control subjects.

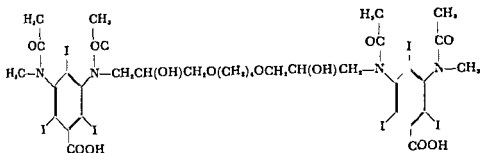
### SUMMARY

The degree of parotid salivary gland involvement in patients with Sjogren's syndrome with or without rheumatoid arthritis has been evaluated by hydrostatic sialography and stimulated flow rate measurements. The results indicate that the latter method provides a more sensitive index of parotid gland dysfunction.

### ZUSAMMENFASSUNG

Der Grad der Beteiligung der Parotis in Patienten mit Sjogrens Syndrom mit oder ohne rheumatoide Arthritis wurde durch hydrostatische Sialographie und Flussigkeitsstrommes-

solution of its methylglucamine salt (Ph DZ 59B) in angiography produced less symptoms and fewer adverse effects on the circulation than certain contrast media currently in use. The chemical structure of Ph DZ 59A is



The practical value of the contrast medium has now been further explored and compared with others, especially as regards its delivery rate through various types of catheters.

**Material and Methods** The first injector used was a Cisol II (Elema Schönder, Solna, Sweden) driven by compressed air. Five injections of every contrast medium were made through each catheter at indicated pressures of 3, 4, 5, 6 and 7 kp/cm. An automatic heating device in the injector kept the temperature at 37° C. The injections were made into a container with the tip of the catheter and the side holes always under the surface of the contrast medium. The injection times were measured by the recording system built into the Cisol injector, a system with an inherent error of + 0.05 s, the times for the different media were calculated and expressed as ml contrast medium or g iodine per second.

Three standard catheters of different sizes for cardioangiography and angiography were used.

(1) Grey Ödman Ledin catheter, length 90 cm, ID 1.8 mm, end hole and four side holes. This catheter is routinely used for cardioangiography and thoracic aortography.

(2) Red Ödman Ledin catheter, length 90 cm, ID 1.15 mm, end hole and four side holes. This catheter is routinely used for selective angiography of various aortic branches.

(3) NIH thin wall woven dacron catheter size 5F, length 80 cm, ID 0.86 mm with closed tip and six side holes (USCI). This catheter is routinely used for cardioangiography in small newborn infants.

Fifty ml of contrast medium per injection were used with the grey Ödman-Ledin catheter, 20 ml with the red Ödman Ledin catheter and 10 ml with the NIH 5F catheter.

## DELIVERY RATES OF CERTAIN CONTRAST MEDIA THROUGH CATHETERS FOR ANGIOGRAPHY AND CARDIOANGIOGRAPHY

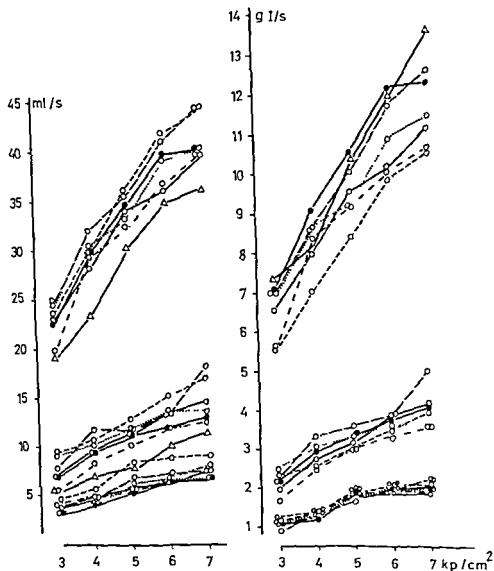
by

LARS BJORK, UNO ERIKSON and ARNE HOLTZ

The quality of an angiogram is determined to a great extent by the size of the patient, the radiographic technique, the flow rate in the vascular system to be examined and the amount of contrast medium or rather the quantity of iodine per second that can be injected into the vessels. The iodine administered depends primarily, of course, upon the inner diameter and length of the catheter, the type of injector and injection pressure as well as upon the iodine content and the viscosity of the contrast medium.

SWARTZ & DINGENDORF (1959), COOLEY & BEENTJES (1963), OLIN (1963) FISCHER (1965), KROVETZ et coll (1966) and others have demonstrated that it is difficult to calculate how much iodine per second can be injected by means of a particular contrast medium of given concentration. Practical tests of the injection rates have to be performed with different types of catheters and injectors.

BJORK et coll (1969) reported that a new contrast medium, Ph DZ 59A (proposed international non proprietary name iozomic acid) when used as a



Injection rates ml/s (left) and g I/s (right) for various contrast media with the Cisl II injector. From above: Grey Ödman Ledin, red Ödman Ledin, and NIH 5F thin wall woven catheters.

— Urografin ● ● Angiografín ○ ○ Conray Meglumín Isopaque Cerebral,  
 Ph DZ 59B 57% Ph DZ 59B 67.8% — — — Ph DZ 59D 58.3%

The following contrast media were investigated

570 mg Ph DZ 59B per ml, iodine content 235 mg per ml Viscosity 5.2 cP at 37° C (Methylglucamine salt of Ph DZ 59A)

678 mg Ph DZ 59B per ml, iodine content 280 mg per ml Viscosity 9.9 cP at 37° C (Methylglucamine salt of Ph DZ 59A)

583 mg Ph DZ 59D per ml, iodine content 280 mg per ml Viscosity 5.1 cP at 37° C (Monoethanolamine salt of Ph DZ 59A)

Isopaque Cerebral, 590 mg methylglucamine metrizoate and 11.3 mg calcium metrizoate per ml, iodine content 280 mg per ml Viscosity 4.0 cP at 37° C (Nyegaard & Co A/S, Oslo)

Conray Meglumín, 600 mg methylglucamine iothalamate per ml, iodine content 282 mg per ml Viscosity 3.7 cP at 37° C (Mallinckrodt Chemical Works Ltd, St. Louis)

Angiografin, 650 mg methylglucamine diatrizoate per ml, iodine content 310 mg per ml Viscosity 4.9 cP at 37° C (Schering AG, Berlin)

Urografin 76%, 100 mg sodium diatrizoate and 660 mg methylglucamine diatrizoate per ml, iodine content 370 mg per ml Viscosity 8.5 cP at 37° C (Schering AG Berlin)

The second injector was the Contrac (Contraves AG, Zurich) driven by an electric motor with an electronic control system that automatically interrupts the flow when the pressure in the injector reaches a safety level of approximately 42 kP/cm<sup>2</sup>. The flow rate desired through any catheter can be selected but is obviously limited by the maximal pressure, as indicated above. By continuously increasing the flow rate until the injections were interrupted by the automatic safety control the maximal flow rate for every contrast medium through each catheter could be determined. Only the red Ödman-Ledin and the NIH catheters were used in this experiment since the maximum flow rate for the grey Ödman Ledin catheter could not be determined.

The red Ödman-Ledin catheter was employed with 20 ml and the 5F catheter with 10 ml of contrast medium. The injections were made into a container with the tip of the catheter and side holes under the surface of the contrast medium, an automatic heating device in the injector kept the temperature constant at 37° C.

Three contrast media were investigated

Ph DZ 59B, 570 mg methylglucamine iozomate per ml, iodine content 235 mg per ml Viscosity 5.2 cP at 37° C

Conray Meglumín, 600 mg methylglucamine diatrizoate per ml, iodine content 282 mg per ml Viscosity 3.7 cP at 37° C

Angiografin, 650 mg methylglucamine diatrizoate per ml, iodine content 310 mg per ml Viscosity 4.9 cP at 37° C

the injection rate. It is obvious that the relationships indicated by the law of Poiseuille do not always exist in the injection systems used. Changes from laminary to turbulent flow may occur to a varying and unpredictable degree in an injection system for contrast media. Practical tests with the catheters to be employed and with the injector available must therefore be performed to determine the flow rates that will be available in particular examinations. It is also clear that catheters, particularly of the disposable type, may vary considerably in diameter, irregularities in stopcock attachments and in the size of the end and side holes may also occur. Data obtained with one catheter are consequently not automatically applicable to another of the same nominal size. The same catheters were used for all injection investigations with the Cisal II injector. The high pressures with the Contrac injector often necessitated the replacement of burst catheters.

Systematic variations in delivery rate from one injection to another occurred with the Cisal II injector. These arose in spite of efforts to maintain the storage tube air pressure above 50 kP/cm<sup>2</sup> and to keep the amount of medium in the injector the same for all injections, variations in injection rates of 20 per cent can be expected. These systematic differences in the performance of the Cisal II injector are probably of little importance in clinical angiography, this injector is not however suitable for investigation in which a more exact dosage of the contrast medium is desired.

The injection rate through a catheter with one injector varied only slightly with moderate variations in viscosity, concentration and iodine content of the solutions with the methylglucamine salts of the contrast media tested. If higher injection rates are desired other compounds of the acids, such as monoethanolamine or sodium salts or mixture of such salts and methylglucamine salts, have to be tried. This is of practical importance, particularly in the smaller vascular beds where the flow rate through them is generally reached by the injection. A further increase in delivery rate through the catheter will then have little effect on the iodine content in the vascular bed, the iodine content in the medium injected has to be increased if the iodine concentration in the vessels is to be raised.

Since it has been proven that the adverse effects of contrast media are a function of the concentration, it is always essential to determine the lowest iodine concentration acceptable for the diagnosis. The estimation requires knowledge of the flow rate in the vascular bed to be examined, a prerequisite that is impossible. An indication however that the maximum flow rate of the vascular bed is reached is the occurrence of back flow from a selectively injected artery into a major artery (OLIN & REDMAN 1966). If this condition is fulfilled and optimal exposure factors are used, a satisfactory angiographic result may usually be expected with a relatively low concentration of contrast medium. On the other

Table

*Maximum delivery rate with the Contrac injector of three different contrast media through a red Ödman Ledin catheter and a NIH woven dacron 5F catheter*

| Contrast medium   | Red Ödman Ledin |       | NIH 5F |       |
|---|-----------------|-------|--------|-------|
|   | ml/s            | g I/s | ml/s   | g I/s |
| Meglumine diatrizoate (650 mg/ml, iodine content 310 mg/ml) | 24              | 7.4   | 15     | 4.3   |
| Meglumine iohalamate (600 mg/ml, iodine content 282 mg/ml)  | 22              | 6.2   | 13     | 3.7   |
| Meglumine iozamate (570 mg/ml, iodine content 235 mg/ml)    | 30              | 7.0   | 17     | 4.0   |

## Results

The results of the determination of injection rates with the *Cisal II* injector appear in the Figure expressed as ml contrast medium and g iodine per second, respectively.

The delivery rate with the two smaller catheters was determined almost entirely by the injection pressure. Almost a linear relationship exists between the injection pressure and the volume of contrast medium delivered through the catheter. With the larger grey Ödman-Ledin catheter the injection rate, expressed as ml/s, was largely dependent on the pressure with slight but not significant variations between the contrast media. A tendency exists for the relationship between injection pressure and injection rate to become non-linear with the higher pressures. The rate when expressed as g iodine/s was again determined essentially by the pressure employed with the two smaller catheters.

The results of the investigations with the Contrac injector are summarized in the Table. The delivery rate through the two relatively small catheters varied little with the different media tested. With the maximum injection pressure for this injector (ca. 42 kP/cm<sup>2</sup>) nearly the same amount of iodine is delivered per second through a given catheter in spite of moderate differences in the concentration and iodine content of the solutions.

## Discussion

The results confirm earlier investigations that indicated that it is difficult to calculate how much contrast medium can be injected through a given catheter with a certain type of injector. They also disclosed that the viscosity of the contrast medium expressed as cP at 37° C is only one of many factors determining

## ANGIOGRAPHY OF THE HIP REGION

Comparison between different angiographic modifications

by

HERBERT MUSSBICHLER

Angiography of the hip region represents an easy and effective way of investigating the vascular anatomy of the femoral head (MUSSBICHLER 1965, 1971). A series of such investigations in living subjects disclosed anatomic variations such as hypoplasia and absence and anomalous origin of the most important afferent artery, the posterior collum branch. Angiography also allowed the demonstration of local vascular lesions in patients with recent or old neck and pertrochanteric fractures (MUSSBICHLER 1956, HIPP *et coll* 1962, BRUGGER 1963, BRUNNER *et coll* 1967, MAURER *et coll* 1969, MUSSBICHLER 1970) as well as with necrosis of the femoral head (MUSSBICHLER 1956, 1970) and Perthes disease (MUSSBICHLER 1956). The angiographic technique however varied somewhat from author to author. Most of them injected contrast medium into the external iliac artery in a retrograde direction while an antegrade technique of injection was practised by MUSSBICHLER (1971). Some of the authors used compression of the femoral artery, while the amount of contrast medium also varied.



hand if the iodine concentration in the vascular bed to be examined should for some reason be unsatisfactory a higher concentration of contrast medium should be employed in subsequent injections

## SUMMARY

Investigations into the injection of various contrast media for angiography including a new agent Ph DZ 59A, indicated that the injection rate varied only little with moderate alterations in their viscosity, concentration and iodine content. Practical tests with the catheters to be used and the injector available, performed to determine the flow rates available in particular examinations are described.

## ZUSAMMENFASSUNG

Untersuchungen über die Injektion verschiedener für die Angiographie vorgesehene Kontrastmittel einschliesslich eines neuen Mittels Ph DZ 59 A zeigten dass sich die Injektionsgeschwindigkeit nur wenig mit geringeren Änderungen der Viskosität Konzentration und dem Jodgehalt ändern. Praktische Tests mit den verwendeten Kathetern und dem verfügbaren Injektor ausgeführt um die resultierenden Flusgeschwindigkeiten bei den einzelnen Untersuchungen zu bestimmen, sind beschrieben.

## RÉSUMÉ

Une étude expérimentale de l'injection de différents moyens de contraste pour angiographie, y compris un nouveau produit Ph DZ 59A a montré que la rapidité d'injection ne varie que quand la viscosité la concentration et la teneur en iode des produits ne subissent que de petits changements. Les auteurs décrivent les tests pratiques qu'ils ont faits pour déterminer les débits que l'on peut obtenir dans certains examens avec l'injecteur qu'ils ont à leur disposition et avec les catheters qu'il faut utiliser.

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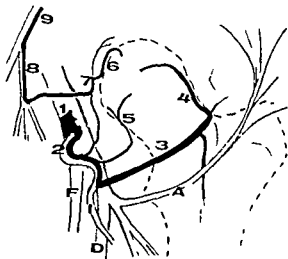


tion of 16 ml Urografin 76 % into the external iliac artery through a straight polythene catheter 20s inserted percutaneously

Semiselective angiography was performed by injecting 10 ml Urografin 76 % antegradely through a looped red Ödman Ledin catheter (Fig 2 b). The jet of contrast medium was thus directed to the external iliac artery and its branches which supply the femoral head.

Compression of the femoral artery was applied by adjusting a blood pressure cuff around the middle of the thigh. Five minutes before the injection the cuff was inflated until pulsation in the dorsalis pedis artery ceased. Urografin 76 % was injected at the rate of about 7.5 ml/s either by hand or an automatic injector (Cisal).

Fig 1 The main arteries of the hip region, vessels directly or indirectly supplying the femoral head. Common femoral artery (1), medial circumflex artery (2), posterior collum branch (3), superior retinacular artery (4), inferior retinacular artery (5), ligamentum teres artery (6), acetabular artery (7), obturator artery (8), internal iliac artery (9). Other arteries: Femoral (F), deep femoral (D), ascending branch of lateral circumflex (A), inferior branch of the medial circumflex artery (1)



The aim of the present investigation was to evaluate the extent to which such modifications of the angiographic technique influence the filling and recognition of the arteries of the femoral head

Anatomic investigations in cadavers (NUSSEBAUM 1926, HOWE et coll 1950, TRUETA et coll 1953, SEWITT et coll 1965) have established that the posterior collum artery, identical with the ramus profundus of the medial circumflex artery, conveys the bulk of the blood to the femoral head (Fig 1). This artery terminates in the superior retinacular artery. The pioneer work of TRUETA & HARRISON (1953) and SEWITT & THOMPSON (1965) established that this artery represents the most important supply to the femoral head while the inferior retinacular and ligamentum teres arteries play only a subsidiary role.

*Material and Methods* Angiography of the hip was performed with the following variations in a material of 59 cases: (1) general and semiselective angiography in 13 cases of normal hips, (2) compression and no compression of the femoral artery in 9 cases, 6 of which had unaffected hips and 3 had coxarthrosis, (3) injections of different amounts of contrast medium in 25 cases, 12 of which had normal hips, 11 coxarthrosis and 2 cases had recent cervical fractures, and (4) the angiographic examination was repeated under identical technical conditions in 12 normal cases.

The angiographic methods and modifications have been partly described in detail in the present journal (MUSSBICHLER 1971). They comprise the following procedures:

Filling of both the external and internal iliac arteries was obtained by general angiography (Fig 2 a). The examination was carried out by retrograde injection



a

b

F C

select (b)  
filled with the  
the branches

Injection of 16 ml Urografin 76 into the external iliac artery through a straight polythene catheter 20 cm inserted percutaneously

Semiselective angiography was performed by injecting 10 ml Urografin 76 % antegradely through a looped red Ödman Ledin catheter (Fig 2 b). The jet of contrast medium was thus directed to the external iliac artery and its branches which supply the femoral head.

Compression of the femoral artery was applied by adjusting a blood pressure cuff around the middle of the thigh. Five minutes before the injection the cuff was inflated until pulsation in the dorsalis pedis artery ceased. Urografin 76 % was injected at the rate of about 7.5 ml/s either by hand or an automatic injector (Cisal).

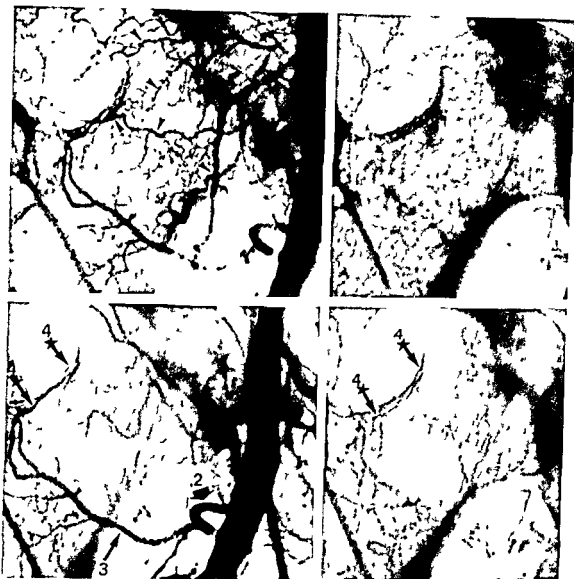


Fig 3 Two series of angiograms of a normal hip from general (upper) and semiselective (lower) angiography. Femoral head vessels in middle and late arterial phase. The superior retinacular artery (4) is evident in the semiselective examination but superimposed by gluteal branches (small arrows) in the general angiography. Medial circumflex artery (2) posterior collum branch (3).

The effect of compression of the femoral artery was tested on the duration of filling of certain vessels of the hip region, such as the common femoral artery at its bifurcation, the medial circumflex artery, the ascending branch of the lateral circumflex artery, the posterior collum branch, the superior retinacular artery and the inferior branch of the medial circumflex artery. The duration of the arterial filling was accounted from the time difference between the



Fig. 4. Subtraction angiograms of normal hip examined by semiselective angiography: first without compression of the femoral artery (left) and with compression (right). In both examinations 10 ml Urografin 6% were injected at the same rate and the exposures made at moments (arrows) corresponding to those in the records. The number of small arteries filled increased when compression was applied.

first exposure in which contrast medium appeared in the trunk of the vessels and the last exposure in which it was still visible in the most peripheral part of the arteries. The figures were assessed by a correlation of recordings of the exposures with the serial angiograms. The superior retinacular artery was measured in the angiograms with a mm rule to indicate the degree of arterial filling, angiographic extension. Serial angiography at a rate of one exposure per second over 15 seconds was performed with an Elema-Schonander AOT filmchanger. All catheters had two sideholes within 2 cm of the tip. Factors: A p 60—80 kV, 64 mAs, 1 s, FFD 100 cm. femoral artery usually compressed.

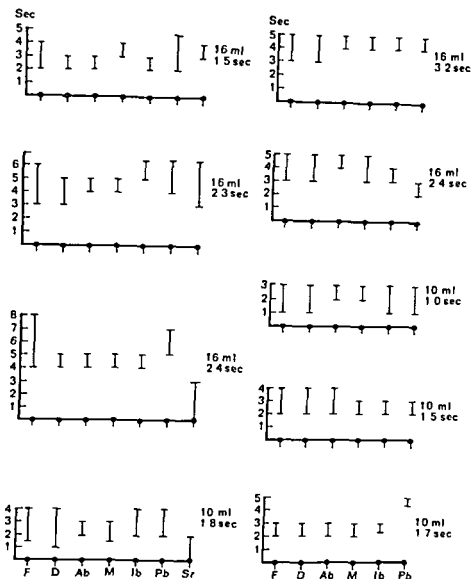


Fig 5 Duration of arterial filling in 9 cases examined first without compression (lower marks) and with compression of the femoral artery (upper marks). The number of ml Urografin 76 injected and the rate of injection is given in each case. The femoral (F) deep femoral (D) ascending branch of the lateral circumflex (Ab) medial circumflex (M) its inferior branch (Ib) posterior collum branch (Pb) and superior retinacular (Sr) arteries were examined. The differences in the duration of filling (indicated by I) between the effect of compression and the absence of compression of the femoral artery is 1 to 4 s in favour of the former.

## Results

Each of the 13 cases was examined twice, first with the general and secondly with the *semiselective* method. The filling frequency of the posterior collum branch and the superior and inferior retinacular arteries was identical in both series. These vessels filled in 13, 11 and 9 cases, respectively. However, the 'angiographic extension' of the superior and inferior retinacular artery was 4 to



Fig 6 Serial angiograms in malrotated femoral neck fracture with injection of 16 ml Urografin 76 % (upper) and 10 ml (lower) Both examinations demonstrate normal and defect filling of the posterior column branch (arrows left and right respectively) indicating intermittently arrested circulation

8 mm greater with the semiselective than with the general method in 5 and 3 cases respectively. On the other hand the acetabular artery could be demonstrated with the general method in 5 cases and with the semiselective procedure in 3 cases only. The recognition and identification of the femoral head vessels was facilitated because of the absence of filling of superimposing gluteal vessels. This concerned mainly the demonstration of the superior retinacular artery (Figs 2, 3).

General angiography was carried out first without compression and then with compression of the femoral artery at the middle of the thigh. The degree and



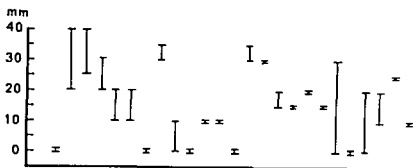


Fig 7 Extension of the superior retinacular artery measured in the angiograms in 25 cases examined with 16 ml Urografin 76 % (upper marks) and 10 ml (lower marks) respectively. The artery filled in 20 cases with the former and in 17 cases with the latter. The extension indicated in mm on the abscissa (indicated by I), differed in 12 cases in favour of the higher amount of medium.

duration of arterial filling, particularly of the smaller vessels, was increased by compression in all 9 cases (Fig 4). The effect was most significant in the femoral and deep femoral arteries where the filling became prolonged for 2 to 4 seconds, the increase in the duration of filling ranged between 1 and 3 seconds in the posterior collum branch (Fig 5).

Each of the 25 cases was injected first with 16 and secondly with 10 ml Urografin 76 %. The posterior collum branch always filled and was of identical length in both series. This was also evident in two recent cervical fractures which were associated with a circulatory disturbance in the posterior collum branch (Fig 6). The superior retinacular artery filled in 20 out of the 25 cases after the injection of 16 ml of medium and in 17 cases after the introduction of 10 ml of medium. The 17 cases in which the artery was filled in both series were compared with the extension evident at angiography. The figures were identical in both series in 8 cases. In the remaining 9 cases the filling of the artery was increased in the 16 ml series as compared with the 10 ml series. The difference was up to 5 mm in 3 cases, 6 to 10 mm in 4 and 11 to 20 mm in 2 cases (Fig 7).

The injection of identical doses of contrast medium was repeated with general angiography in 12 cases 1.5 to 6 months later, 16 ml Urografin 76 % being injected over 2 to 3 seconds by hand. The filling frequency was identical in both series of examinations. The posterior collum branch filled in all but 1 case in which it was of anomalous origin. The superior retinacular artery could be demonstrated in 8 cases, the inferior retinacular artery in 6 and the acetabular artery in 4 cases. The extension of the arteries, measured from identical projections was identical, i.e. within the range of 3 mm in the two angiographic series.

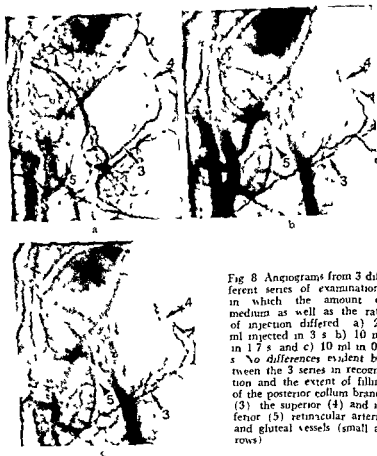


Fig 8 Angiograms from 3 different series of examinations in which the amount of medium as well as the rate of injection differed: a) 20 ml injected in 3 s b) 10 ml in 17 s and c) 10 ml in 0.7 s. No differences evident between the 3 series in recognition and the extent of filling of the posterior collum branch (3) the superior (4) and inferior (5) retinacular arteries and gluteal vessels (small arrows).

### Discussion

Previous angiographic investigations of normal hips in living subjects indicated that filling of the femoral head vessels was not always obtainable (MUSSBICHLER 1956, BRUGGER 1963, MUSSBICHLER 1971). MUSSBICHLER (1971) in an investigation comprising angiography of 92 such hips was able to fill the superior retinacular artery in 69 per cent of the cases, the inferior retinacular artery in 63 per cent and the acetabular artery in up to 40 per cent of the cases. He further observed that the posterior collum branch was absent in 9 cases. These findings lead to a consideration of whether non-filling of arteries is a result of a deficient angiographic technique and so to whether the arterial filling can be improved.

The results of the present investigation indicate that recognition and extension of the posterior collum branch is not influenced by the various angiographic modifications tested. This means that non-filling of this artery in fact indicates its absence. This is also stressed by these findings being bilateral (MUSSBICHLER 1971).

The frequency and recognition of the filling of the superior retinacular artery responsible for the nutrition of the femoral head, was clearly favoured by use of the semiselective method, compression of the femoral artery and a higher dose of contrast medium. However, there were always some cases in which the artery could not be demonstrated with any of the angiographic modifications used. The non-recognition of the vessel is supposed to be due to its small calibre, 0.3 mm representing the lower limit of radiographic demonstration. This may also explain the limitation of filling of the other femoral head vessels, i.e. the inferior retinacular and the acetabular arteries.

The findings also indicate that an increase in the amount of contrast medium not necessarily favours the demonstration of the femoral head vessels (Fig. 8), from this it may be concluded that the optimal dose of medium depends on the individual properties or conditions of the vessels examined. Non-recognition of the superior retinacular artery in fractures of the neck or other pathologic conditions must therefore not be interpreted as indicating vascular damage of the femoral head, angiographic demonstration of the artery may however suggest that the blood supply to the head is preserved or intact.

## SUMMARY

The use of semiselective (antegrade) angiography with compression of the femoral artery proved to be the best technique for demonstrating the vascular supply of the femoral head. However, the superior retinacular artery did not fill in all cases examined whether 10 ml or 16 ml of contrast medium were injected. This fact should be taken into account in interpretation of angiograms from cases with hips affected by fracture or other diseases. Control examinations proved the reliability of the angiographic method.

## ZUSAMMENFASSUNG

Die Anwendung der semiselectiven (antegraden) Angiographie mit Kompression der Femoralarterie erwies sich für die Darstellung der Gefäßversorgung des Femurkopfes am erfolgreichsten. Trotzdem war es nicht in jedem Falle möglich die Arteria retinacularis superior abzubilden, nicht einmal dann wenn die Kontrastmitteldosis von 10 ml auf 16 ml erhöht wurde. Dieser Umstand ist bei der Beurteilung von Angiogrammen von Fällen mit Collumfraktur oder Hüfterkrankungen zu berücksichtigen. Mittels Kontrolluntersuchungen wurde die Zuverlässigkeit der angiographischen Methode bewiesen.

# RÉSUMÉ

L'angiographie semi selective (anterograde) avec compression de l'artere femorale s'est révélée être la meilleure technique pour mettre en évidence l'apport vasculaire a la tête du femur. Cependant l'artère epiphysaire superieure n'est pas visible dans tous les cas examines, que la quantité de contraste injectée soit de 10 ml ou de 16 ml. Il faut tenir compte de ce fait pour interpréter les angiographies de cas de hanches atteintes de fracture ou d'autres affections. Des examens de contrôle ont montre que la methode angiographique est fiable.

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## INJECTION OF CONTRAST MEDIUM INTO UNSTAINED FEMORAL LYMPH VESSELS FOR LYMPHOGRAPHY

A new technique and its indications

by

OLUF MYHRE

Lymphography has in recent years become a routine procedure of investigating the lymph structures of the pelvis and retroperitoneum in malignant lymphoma and certain forms of carcinoma. The contrast medium is usually injected via lymph vessels in the dorsum of the foot by the method described by KREMENTZ (1952). TJERNBERG (1962) inserted a fine plastic catheter into the lymph vessel instead of puncturing it with a cannula. These methods necessitate staining of the lymph vessels with Patent Blue, injected distally in the dorsum of the foot. A contrast medium of fairly high viscosity (ultra fluid lipiodol) is generally used, and often causes a considerable pressure increase in the lymphatics of the lower extremities during the injection.

BRUN & ENGESET (1956), and later HALL & KREMENTZ (1967), injected the contrast medium into inguinal lymph nodes, either by the percutaneous route or after incision under local anesthesia. This method has not been widely accepted, probably because extravasation of the medium often occurs, such a mishap

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prevents exact regulation of the amount injected and the procedure cannot be used when metastases are present in lymph nodes in the groin

ABERNATHY *et coll* (1967) described a technique for injecting contrast medium into unstained femoral lymphatics in dogs, pointing out that the lymph vessels are wider proximally in the extremities and that there is a lower resistance to injection in those regions, deep incisions, 3 to 4 cm long, were used however

*Injection of contrast medium into the foot* Puncture is unsuccessful in roughly 5 per cent of examinations, according to FLEISCH (1965), and in roughly 1 per cent, according to TURNER (1968)

Even when a lymph vessel in the foot has been successfully punctured the examination cannot be carried out if any appreciable subcutaneous extravasation of contrast medium is present in the lower leg or thigh, and must be broken off if any lymphovenous anastomoses should be observed These problems arise most frequently in elderly patients An injection into the foot is difficult to perform or contra indicated in severe dermatitis, indurated edema, or when there is widespread scarring on the dorsum Hypersensitivity of Patent Blue, observed at an intracutaneous test before a planned lymphography, constitutes a problem in some patients because unstained lymphatics in the foot are not easily localized and punctured

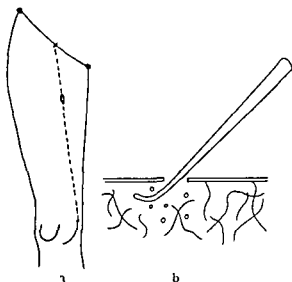
The writer considers that injection in the femoral region is indicated when lymphography cannot be carried out via the foot because of one or several of the aforementioned difficulties.

#### *Injection of contrast medium*

lymphatics in the femoral region are found in the upper thigh they follow the great saphenous vein, but course slightly lateral to that vessel, and are more superficial lying 0.5 to 1.5 cm below the corium Lymph vessels, 1 to 1.5 mm in diameter occur in this region

The procedure is carried out under local anesthesia with 6 to 8 ml xylocaine 1% injected subcutaneously A 0.8 to 1 cm longitudinal incision (Fig 1a) is made to correspond with the course of the above mentioned lymph vessels and, after the corium has been opened, the subcutis is incised vertically with curved Pean's forceps A pair of curved anatomic eye forceps are now inserted so that their tip lies 0.5 to 1 cm deep in the subcutis (Fig 1b), they are lifted slowly out of the wound, held in a horizontal position when one or two lymph vessels will usually ride over the instrument The vessels are readily freed from fatty tissue and are then seen to have a slightly irregular calibre and contain colourless fluid A lymph vessel is stretched over the two blades of the scissors, punctured

Fig 1 a) Site of incision for injection of contrast medium into a subcutaneous lymph vessel in the thigh. A line is drawn from the middle of the inguinal ligament to the medial aspect of the knee. An incision 0.8 to 1 cm long is made along this line, approximately 10 cm distal to the symphysis pubis. b) Schematic drawing of subcutaneous lymph vessels (small circles), one of which lies in the concavity of the curved forceps.



with the 'shoe horn' instrument described by TJERNBERG (1962), and a 0.6 mm polythene catheter with the end cut off obliquely inserted along the concavity of the instrument (Fig 2). After the catheter has been pushed into the lymph vessel for a distance of 3 to 5 mm the puncture instrument is withdrawn and a fine silk ligature passed around the lymph vessel and the catheter. The eye forceps are now removed and the catheter is connected to an injection syringe mounted vertically on a stand and with the piston weighted.

After about 0.5 ml of contrast medium has been injected a roentgenogram of the inguinal region is obtained to make sure that no paravasal or intravenous injection has taken place. The customary amount of 4 to 6 ml of contrast medium for a lower extremity is introduced over a period of 30 to 50 minutes.

**Material and Results** A total of 332 lymphographies were performed during the period July 1967—April 1970 to investigate the pelvic and retroperitoneal lymph nodes. The referring diagnoses, in order of frequency, were malignant lymphoma, carcinoma of the urogenital region, and carcinoma of the large bowel.

An attempt was always first made to carry out the examination via lymphatics of the foot; this was successful in 643 lower extremities or 96.8 per cent out of a total of 664 limbs. The reasons why the contrast medium could not be injected via the foot in 21 limbs (3.2 per cent) were as follows: (A) extravasation of contrast medium in the leg and thigh—10 extremities (1.5 per cent), (B) unsuccessful puncture of lymphatics of foot—8 extremities (1.2 per cent), (C) lymphovenous anastomosis distally in thigh—1 extremity, (D) lymphatic stenosis in thigh (post-traumatic)—1 extremity, and (E) scarring on foot

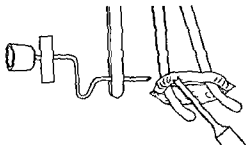


Fig 2 A lymph vessel has been pulled out and is lying over the curved forceps. The puncture instrument has been inserted into the vessel and the 0.6 mm OD catheter introduced with the aid of anatomic forceps. The catheter with the end cut off obliquely is attached to the skin with tape.

following three attempts at lymphography at another hospital—1 extremity

Injection of contrast medium in the femoral region was performed in 10 patients, or 11 lower extremities in all, and was successful in 10, one puncture failed because of fragile lymphatics. These patients were all over 50 years of age. The previously mentioned problems connected with injection in the foot constituted the indications for these femoral injections, 5 of which may be referred to group A, 3 to group B, and 1 to each of groups C, D and E.

As a result of the femoral injections the proportion of unsuccessful examinations in the total material could be reduced from 32 to 17 per cent. No complications were observed after the interventions in the femoral region.

### Discussion and Conclusions

Injection of contrast medium via the foot in a large series of lymphographies occasionally fails, either because of the age or general condition of the patient, or because the examiner lacks experience. It must be stressed that of all the problems connected with the injection in the present material, less than half were due to puncturing difficulties while leakage, lymphovenous anastomosis, lymphatic stenosis and scarring of the foot were the main causes.

Injection in the femoral region may be used as a supplementary procedure, and possesses advantages in that the lymphatics located proximally in the thigh are of wider calibre than those in the foot and the injection may be performed more rapidly owing to reduced resistance. One disadvantage is that the lymph vessels in the thigh do not permit staining, and that wider experience is needed for success than in lymphographies via the vessels in the foot.

The lymphatics are to be preferred to the lymph nodes because of frequent leakage of the contrast medium from the latter in spite of a slow rate of administration. This method often also requires surgical exposure of a lymph node when percutaneous puncture is not possible.



## Addendum

A further 5 lymphographies with injection into the thigh were carried out between April 1970 and September 1970 and produced adequate results. A total of 16 femoral injections has now been reached with only one failure.

## SUMMARY

The technique and indications for lymphography after injection of contrast medium into lymph vessels in the thigh are described and discussed. Injection in the femoral region was performed in 10 cases in which the examination could not be undertaken by injection into lymphatics of the foot. The proportion of unsuccessful injections was thereby reduced from 3.2 to 1.7 per cent in a series of 332 lymphographies.

## ZUSAMMENFASSUNG

Die Indikationen und die Methodik für die Lymphographie nach Kontrastinjektion in die Lymphgefäße des Oberschenkels werden beschrieben. Diese Form der Lymphographie wurde 332 mal vorgenommen in 10 Fällen weil eine Injektion in die Lymphgefäße des Fußes unmöglich war. Mit Hilfe der neuen Methode konnten misslungene Injektionen bei der Lymphographie von 3,2 Prozent auf 1,7 Prozent reduziert werden.

## RÉSUMÉ

Description et étude de la technique et des indications de la lymphographie par injection d'un moyen de contraste dans les vaisseaux lymphatiques de la cuisse. L'injection dans la région fémorale a été faite dans 10 cas où il était impossible de la faire dans les lymphatiques du pied. Sur une série de 332 lymphographies au pied la proportion des échecs d'injection a été ainsi réduite de 3,2 à 1,7 pour cent.

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## LYMPHOGRAPHY IN THE TREATMENT OF CARCINOMA OF THE VULVA

by

STEINAR HAGEN and RAGNAR BJORN-HANSEN

Direct lymphography has been used extensively in diagnostic radiology since KIMMOTH 1955 described his technique. The detection of impalpable lymph node metastases should prove the method to be of value although conflicting results have been reported. Some authors describing metastatic lymph node involvement in carcinoma of the cervix and vulva claim that the accuracy of lymphography is high (AVERETTE et coll 1964, COMAS et coll 1969, GERTEIS 1967) while others are less enthusiastic (JACKSON 1967, REIFFENSTUHL 1967, RITTMANN & WIETH 1968). FLUCHS (1969) surveyed the literature and described his own series of investigations. He concluded that the method is of little value where the inguinal nodes are concerned although it appears to be the only way of detecting metastatic spread to the external iliac lymph node groups.

The purpose of the present paper is to report experiences with lymphography as a pretherapeutic examination in patients with carcinoma of the vulva.

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Table

*Correlation between histologic and lymphographic findings in a total of 102 inguinal and pelvic lymph node regions*

| Lymphographic findings | Histologic findings |          |               |          |
|------------------------|---------------------|----------|---------------|----------|
|                        | Inguinal region     |          | Pelvic region |          |
|                        | Negative            | Positive | Negative      | Positive |
| Negative               | 35                  | 6        | 32            | 0        |
| Uncertain              | 7                   | 0        | 9             | 0        |
| Positive               | 6                   | 1        | 5             | 1        |
| Total                  | 48                  | 7        | 46            | 1        |

**Material and Methods** Lymphography was performed preoperatively in a series of 29 consecutive patients with malignant tumours of the vulva. Histology revealed squamous cell carcinoma in 27 and malignant melanoma in 2 of the patients. A modification of the technique described by KINMOTH et coll. was used with *Ethiodol* as contrast medium. In one patient the injection of contrast medium was effected on one side only, bilateral lymphograms were obtained in all the others.

The injection was stopped when the contrast medium was demonstrated by fluoroscopy to have reached the lower end of the thoracic duct. Ap and oblique roentgenograms of the inguinal regions, pelvis and abdomen were obtained immediately after completion of the injection in all patients. The same films were repeated the following day. *Ethiodol* combined with chlorophyll was injected on one side in 8 patients while *Ethiodol* by itself was used on the other side. This was done in order to see if the green staining of the nodes could be of some help to the surgeon during the lymph node dissection. An investigation of the effect of chlorophyll on the lymphograms was also required from a radiologic point of view.

Radical vulvectomy with bilateral groin and pelvic lymph node dissection as a single stage procedure was performed in 24 patients. Lymphadenectomy was carried out in one patient on one side only and in 4 other patients the dissection was limited to the inguinal glands (superficial and deep). The different groups of lymph nodes were labelled anatomically as they were removed and roentgenograms of the operation specimens were obtained for further localization and identification of the individual lymph nodes evident in the preoperation films. This was followed by a thorough search for nodes that possibly might not have taken up contrast medium. All nodes were labelled for exact correlation with



Fig 1 Lymphograms classified as positive. Irregular filling defects (arrows) which however were due to degenerative changes. Ethiodol with chlorophyll. Left: Day of injection. Right: Following day.

the results of histologic examination. For the sake of simplicity, the *node regions* will be divided into inguinal and pelvic on the two sides.

The preoperation roentgenograms were classified as positive when *nodes* according to generally accepted criteria were considered to indicate neoplastic involvement. The most important of these criteria were (1) *marginal filling defects* demonstrated both in the filling and the retention phases, (2) *retention* of contrast medium in the afferent lymphatic vessels, (3) *complete blockage* of the afferent vessels with formation of collaterals. The term 'uncertain' was used where the lymphograms could not be classified as definitely positive or negative.

### Results

Satisfactory contrast filling of the lymph nodes was obtained in a total of 114 regions. Four regions were filled in one patient. These were made up of two inguinal regions (right and left), consisting of all superficial and deep groups of nodes and two pelvic regions (right and left) comprising all the lymph nodes located along the external iliac vessels down to the femoral canal as well as the obturator lymph nodes.



Fig 2 Lymphogram obtained 3 days after injection of Ethiodol on the left and this contrast medium with chlorophyll on the right side demonstrating retention in the lymphatic vessels on the right side The filling defects on the left side (arrows) were classified as uncertain and histologic examination revealed degenerative changes



Fig 3 Lymphograms (Left Day of injection Right Following day ) Filling defects in several nodes (arrows) sharp diffuse marginal and others more centrally located Degenerative changes were the only histology findings Similarity to fig 4 evident



Fig 4 Lymphograms (Left Day of injection Right Following day) Sharp marginal filling defect in one iliac node (arrow) due to metastatic involvement The contrast filled vessels cover the filling defect in the roentgenogram taken on the day of injection

Fifty five inguinal and 47 pelvic regions were investigated both by histology and lymphography (cf Table). Metastases to the inguinal nodes were evident in 7 patients and to the pelvic nodes in one patient. It was disappointing to find that lymphography revealed only one of the 7 cases in the inguinal node group. The false positive rate was 6 out of 48 inguinal regions and 5 out of 46 pelvic regions. In addition the number of lymphograms labelled 'uncertain' in the two regions were 7 and 9 respectively. The histologic investigation of the nodes from the false positive group disclosed fibrolipomatosis or reactive changes only. Some examples of the lymphographic findings in the different categories listed in the Table.

**I. Superficial nodes**  
 In the superficial group nodes in this region failed to fill with Ethiodol in several patients (Figs 5 and 6).

Chlorophyll dissolved in the contrast medium consistently disclosed considerable retention of the latter in the lymphatic vessels (Figs. 1 and 2). This often lasted for more than a week, and as the nodes might still be obscured, made the interpretation of the lymphograms difficult. Extravasation of the contrast medium, especially in the thighs, sometimes also occurred on the side on which chlorophyll was used. In addition the surgeons failed to be impressed by the green staining of the nodes; this was particularly true for the inguinal nodes, both superficial and deep, because dissection in this region is performed en bloc



Fig 2 Lymphogram obtained 3 days after injection of Ethiodol on the left and this contrast medium with chlorophyll on the right side, demonstrating retention in the lymphatic vessels on the right side. The filling defects on the left side (arrows) were classified as 'uncertain', and histologic examination revealed degenerative changes.



Fig 3 Lymphograms (Left: Day of injection; Right: Following day). Filling defects in several nodes (arrows): sharp, diffuse, marginal and others more centrally located. Degenerative changes were the only histology findings. Similarity to fig 4 evident.



Fig 6 Lymphogram with medium persisting in the vessels on the right side 24 hours after injection (arrows) Histology Fibrolomatous degeneration of nodes in the deep inguinal group The left side was regarded as normal but neoplastic tissue was present in three inguinal nodes not demonstrated in the lymphogram

changes are evident in the latter phase only (GERTEIS 1967, WALLACE & JACKSON 1968) This observation has not been confirmed in the present series Defects due to metastatic involvement may be obscured by lymph vessels heavily loaded with contrast medium in the films taken during the filling phase WILLIAMS

106  
The present investigation revealed that it may sometimes be impossible to measure the size of the nodes in two projections due to overprojection of other nodes filled with contrast medium

The problem of lymph nodes failing to fill has been a discussion point ever since the method of direct lymphography was introduced in 1955 Attention has especially been focussed on the obturator group The authors feel that this group may usually be demonstrated Perhaps more important where carcinoma of the vulva is concerned is the fact that the superior superficial inguinal nodes are not often evident in the lymphograms





Fig 5 Roentgenogram of operation specimen. Several nodes loaded with contrast medium with some clear nodes in the superior superficial inguinal group. Histology disclosed metastases in two of these latter.

### Discussion

The frequency of lymph node metastases in the present series, excluding the 2 patients with malignant melanoma, was 30 per cent, which is in the same range as reported by WAI (1954). Although the number of patients examined is relatively small, some comments appear to be justified. There seem to be two main difficulties involved in lymphographic evaluation of metastatic spread from malignant tumours of the vulvar region: (1) It may be impossible to distinguish between *roentgenographic changes produced by fibrolipomatous degeneration* and those caused by metastases, (2) the superior superficial inguinal nodes are not often demonstrated by foot lymphography because they drain the buttock region although they may be involved by direct metastatic spread from the inferior group.

Patients with carcinoma of the vulva belong to an age group in which degenerative changes frequently are encountered in the inguinal lymph nodes. The occurrence of fibrolipomatosis is of particular significance, as pointed out by several investigators (FISCHEK et coll 1962, TUCHS 1969). Fig 7 depicts this type of lesion with the corresponding roentgenogram of the operation specimen.

Some authors stress that neoplastic involvement of the lymph nodes produces defects both in the filling phase and in the retention phase, while degenerative

## ZUSAMMENFASSUNG

Es wird eine lymphographische Untersuchung von 29 Patienten mit malignen Tumoren der Vulva vorgelegt. Die Ergebnisse deuten darauf hin, dass die Lymphographie von geringem Wert oder ohne Wert ist. Lymphknotenmetastasen bei dieser Erkrankung festzustellen. Die Zahl falscher negativer und falscher positiver Ergebnisse ist zu hoch. Im Kontrastmittel gelöstes Chlorophyll machte die Deutung noch schwieriger und war ohne wesentliche Hilfe bei der Dissektion.

## RÉSUMÉ

Les auteurs présentent les examens lymphographiques de 29 malades atteintes de tumeurs malignes de la vulve. Les résultats de cette étude montrent que la lymphographie a peu d'intérêt ou n'a pas d'intérêt pour rechercher les métastases ganglionnaires lymphatiques dans cette affection car le nombre des faux résultats négatifs et positifs est trop élevé. La chlorophylle dissoute dans le moyen de contraste a rendu l'interprétation encore plus difficile et n'a pas aidé appréciablement la dissection.

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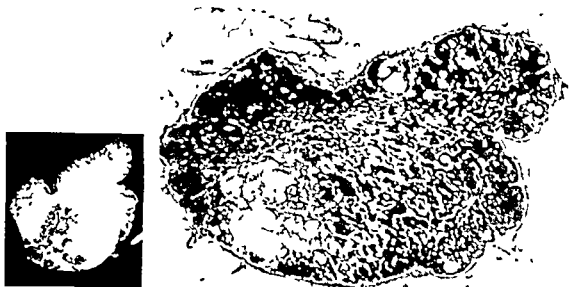


Fig 7 Left Filling defect in a lymphogram of an operation specimen Right Fibrolipomatous changes corresponding to the defect

Stasis in the afferent lymph channels does not necessarily mean neoplastic involvement. This is demonstrated in the case of Fig 6 in which fibrolipomatous degeneration was present on the right side only. On the left side, however, where no stasis occurred, metastases were evident in three inguinal nodes.

It may be concluded that lymphography is of little value in revealing lymph node metastases arising from malignant growths of the vulva, the number of false positive and false negative findings are too high. The experience of the authors with chlorophyll is in full agreement with that of LEMOV *et coll* (1966), and it is felt that it possesses no advantages in lymphography.

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### SUMMARY

A lymphographic investigation of 29 patients with malignant tumours of the vulva is presented. The results indicate that lymphography is of little or no value in disclosing lymph node metastases in this disorder, the number of false negatives and false positives being too high. Chlorophyll dissolved in the contrast medium made the interpretation even more difficult and failed appreciably to aid in the dissection.

## FIBROMUSCULAR HYPERPLASIA AND STATIONARY WAVES OF THE INTERNAL CAROTID ARTERY

by

P R S KISHORE, J P LIN and I I KRICHEFF

Since the first published case report of fibromuscular hyperplasia of the internal carotid artery by CONNETT & LANSCH in 1965, several reports have appeared in the literature describing this entity (1, 4, 6, 11, 16, 18). While the first reported case was proven by histologic examination, in the later reports, except in 6 cases (1, 4, 6, 18), the diagnosis of fibromuscular hyperplasia was made only on the angiographic 'corrugated' appearance of the artery. Of the three cases reported by PALUBINSKAS *et coll* (1966) one had proven fibromuscular hyperplasia of the renal arteries and the other two had no evidence of this entity except the corrugated appearance of the internal carotid artery considered typical for fibromuscular hyperplasia. ANDERSEN (1970) recently reported four cases of fibromuscular hyperplasia with histologic proof in two cases. He also refers to the association of aneurysms and fibromuscular hyperplasia. Houser & Baker 1968 reviewed more than 5 000 cerebral angiograms and they concluded that 16 of their cases had involvement of the extracranial internal carotid artery by fibromuscular hyperplasia based on the 'corrugated' appearance seen on angio-

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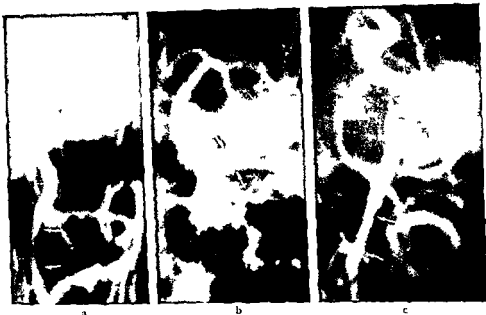


Fig 1 a) Left carotid angiography revealing smoothly narrowed segment of internal carotid artery about 2 cm from origin b) Internal carotid artery within the carotid canal has normal caliber  $\rightarrow$  c) Right biachial angiography in the same patient revealing the smooth concentric stenosis of right internal carotid artery

*Surgical findings* Surgical exploration of the left internal carotid artery revealed its wall to be thickened. The intima was smooth with no evidence of atherosclerosis. The lumen of the narrowed segment only admitted the tip of a number 12 catheter. A minute atherosclerotic plaque was noted at the common carotid bifurcation, but this was over 2 cm away from the narrowed segment of the internal carotid artery. Biopsy of the narrowed segment, endarterectomy, and autologous saphenous vein angioplasty were performed. The patient was discharged without neurologic deficit after an uneventful post operative course.

Microscopic examination revealed proliferation of the smooth muscle of the media. There was no aneurysmal outpouching of the media and the intima was intact. There was no evidence of atherosclerotic changes. These findings were described as compatible with fibromuscular hyperplasia.

### Discussion

The etiology of fibromuscular hyperplasia is unknown although a familial etiology has been reported (Graham et coll (1965)).

It occurs in all

graphy During their investigation they recognized two cases of so called stationary arterial waves in patients with cerebral edema The similarity between the roentgenographic appearance of fibromuscular hyperplasia and stationary waves and the possibility of their being mistaken for each other had been correctly raised by MAYALL and others (3, 14, 15)

THEANDER (1960) was the first to describe stationary arterial waves in peripheral vessels proximal to an occlusion He suggested that the pulse waves were reflected to cause a standing wave appearance which in cases of distal occlusion would be further amplified by resonance WICKROM & BARTLEY (1957) considered stationary waves to be produced by arterial spasm based on their disappearance following administration of vasodilator drugs in one case Since then others have observed this phenomenon and have offered numerous theories as to their etiology and significance (10, 13, 15, 19)

The purpose of this communication is to report a case of fibromuscular hyperplasia of the internal carotid artery, proven by microscopic examination, which has no similarity in angiographic appearance to the frequently described fibromuscular hyperplasia and to discuss the features of this disease which distinguish it from the phenomenon of stationary waves

### Case report

A 42 year old female was admitted to University Hospital with a history of three hour episode of central loss of vision in the left eye speech difficulty and right upper extremity paresis occurring three weeks before admission She experienced a similar episode associated with temporal headache three days later necessitating subsequent admission to the hospital There was no history of other neurologic complaints hypertension or diabetes Physical examination including neurologic status was unremarkable Blood pressure and blood sugar were within normal limits There was no carotid bruit or papilledema Laboratory work including EKG and CSF examination were normal Roentgenograms of the skull were normal EEG showed a left hemispheric focus with slowing Ophthalmodynamometry left eye 50/15 mm Hg and right eye 105/40 mm Hg

*Angiography* Left carotid angiography revealed a relatively smooth 50% narrowing of the left internal carotid artery from about 2 cm above its origin to the level of C1 (Fig 1 a, b) where the artery regained its normal caliber The common carotid artery, external carotid artery and the intracranial arteries were normal The left vertebral artery, examined by left brachial angiography, was normal

Similar changes were found in the right internal carotid artery at right retrograde brachial angiography (Fig 1 c) but the stenosis was slightly less — about 40% The right common carotid artery, external carotid artery, vertebral artery and basilar artery as well as the intracranial arteries were normal



Fig 2 a) Right carotid angiography performed in a 16-year-old male with intracranial aneurysm revealing corrugated appearance of the internal carotid artery. b) Repeat angiography a few minutes later in oblique projection revealing diminution in corrugation and that this is a flow phenomenon—stationary waves. c) Right carotid angiography 9 months later. Right internal carotid artery is normal.

NEW (1966). It is, of course, not difficult to differentiate between uniformly regular arterial waves and a fairly advanced multifocal stenosing fibromuscular hyperplasia. HOUSER & BAKER (1968) emphasized the very regular appearance of stationary waves as a feature to distinguish them from fibromuscular hyperplasia. However, cases in which the amplitude of the arterial waves is large and irregular should not be mistaken for fibromuscular hyperplasia. Under such circumstances a second injection of contrast medium or a repeat examination is extremely helpful in confirming or excluding either diagnosis. In the repeat angiogram, there will be no changes in the organic lesion but some degree of change in the appearance of the vessel in cases of stationary waves as demonstrated by the following case.

A 16-year-old male was admitted to Bellevue Hospital in June 1968 for angiographic evaluation of his status following intracranial clipping of a right middle cerebral aneurysm. His medical history dated back to 1964 when he contracted rheumatic fever with arthritis. In 1967 he had an episode of subarachnoid hemorrhage secondary to right middle cerebral mycotic aneurysm. Intracranial clipping of this aneurysm was performed at that time.

Right carotid angiography performed in June 1968 revealed a corrugated appearance of the internal carotid artery in the distal cervical portion with narrowing of the lumen starting about 2 cm from the origin (Fig 2 a). There was no difficulty in arterial puncture.



age groups ranging from 17 months to 72 years, but it is usually seen in the young and middle age groups (2nd and 5th decades) (10, 16)

WELLINGTON (1963) described two distinct types—one consisting primarily of irregular thickening of the media caused by proliferation of smooth muscle and fibrous tissue and a second type with primarily subadventitial fibrosis. HARRISON *et al.* (1967) in a series of 66 cases of fibromuscular dysplasia of the renal arteries with histologic diagnosis, have clearly noted three morphologic appearances—focal, multifocal and tubular or concentric stenosis. The multifocal type, which is by far the most common type, is the one that gives rise to the 'corrugated' or 'pleated' or 'string of beads' appearance. This appearance of the arteries on angiograms has been considered typical for fibromuscular hyperplasia in the internal carotid arteries (1, 11, 16). In the tubular type, which is the second most common in the renal artery, according to HARRISON *et al.* (1967) a smooth stenosis of the involved vessel will be observed. It was seen in 14 of the 60 cases of medial hyperplasia and subadventitial fibrosis in their series. The case of fibromuscular hyperplasia of the carotid artery we have described is of the tubular or concentric type, with no gross disruption or aneurysmal dilatation and to our knowledge this is the first case reported in the internal carotid artery.

Although the so-called stationary arterial waves of the internal carotid artery are no longer a total enigma (7), the exact nature of their origin still remains unclear. Several theories have been offered to explain their occurrence (13, 14, 15, 19, 21, 23). While none of the theories have explained this phenomenon completely, it would be safe to assume that it is the result of altered hemodynamics. Most reports clearly point out this fact, noting that stationary waves usually occur in the presence of a distal occlusion of the internal carotid artery, an intracranial aneurysm with or without subarachnoid hemorrhage, a previous history of subarachnoid hemorrhage without a demonstrable cause, or increased intracranial pressure (3, 11, 13, 16).

*Angiographic appearance of stationary waves versus fibromuscular hyperplasia*  
The similarity in the angiographic appearance of stationary waves and multifocal fibromuscular hyperplasia is demonstrated by the common use of words like 'corrugated' or 'string of beads'. SZILAGI (1962) obviously mistook stationary waves for fibromuscular hyperplasia. The analysis of angiographic reports of fibromuscular hyperplasia of the internal carotid arteries is made complicated by the reported increased incidence of intracranial aneurysms (1, 3, 16) in patients with angiographically diagnosed fibromuscular hyperplasia, and the association of stationary waves with aneurysms. In view of this increased incidence of stationary waves in patients with intracranial abnormalities, the diagnosis of fibromuscular hyperplasia made by angiography alone, in such instances is open to question. This was demonstrated by BELBER & HOFFMAN (1968) and by



An oblique view performed subsequently to evaluate the aneurysm revealed the corrugations to have diminished considerably (Fig 2 b) Right carotid angiography in March 1969 revealed the extracranial internal carotid artery to be normal (Fig 2 c)

We have seen this phenomenon in four other cases a patient with a malignant mass in the right temporal lobe, a patient with a bleeding posterior communicating aneurysm and subdural hematoma, a patient with subarachnoid hemorrhage from an anterior communicating aneurysm and a patient with pseudo tumor cerebri

Tubular or concentric fibromuscular hyperplasia has no similarity in appearance to stationary waves The smooth narrowing of the artery is similar to changes seen with arteriosclerotic narrowing Angiographically we see no way to distinguish these two diseases However, a strong suggestion of the nature of the lesion may be a narrowing of the internal carotid artery not involving the bifurcation, the usual area for arteriosclerotic changes, particularly in a young patient with otherwise normal vessels this may be something other than arteriosclerosis The differential diagnosis in such cases includes vasculitis, e g giant cell arteritis, which can be excluded on clinical grounds

## SUMMARY

A histologically proven case of fibromuscular hyperplasia of the internal carotid artery in a 42 year old female with cerebral vascular insufficiency is reported The angiographic appearance was not the so called typical but a tubular or concentric stenosis Angiographic features of fibromuscular hyperplasia and their distinction from the so called stationary waves are discussed

## ZUSAMMENFASSUNG

Ein histologisch nachgewiesener Fall von fibromuskulärer Hyperplasie der Arteria carotis interna bei einer 42 Jahre alten Frau verbunden mit cerebraler vaskulärer Insuffizienz wird beschrieben Das angiographische Bild war nicht sogenannten typisch sondern zeigte eine tubuläre oder konzentrische Stenose Die angiographischen Zeichen der fibromuskulären Hyperplasie und deren Unterscheidung von sogenannten stationären Wellen werden diskutiert

## RÉSUMÉ

Présentation d'un cas histologiquement prouvé d'hyperplasie fibromusculaire de l'artère carotide interne chez une femme de 42 ans atteinte d'insuffisance vasculaire cérébrale L'aspect angiographique n'était pas ce qu'on appelle l'aspect typique mais une sténose tubulaire ou concentrique Les auteurs étudient les caractères avec ce qu'on appelle les ondes stationnaires

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Table 1  
*Definitive diagnoses*

| Definitive diagnosis                               | Contrast medium |            |       |
|--|-----------------|------------|-------|
|  | Hypaque 43 %    | Conray 280 | Total |
| Ruptured aneurysm                                  | 6               | 7          | 13    |
| Cerebral haemorrhage                               | 0               | 2          | 2     |
| Cerebral tumour                                    | 2               | 4          | 6     |
| Cerebral thrombosis                                | 1               | 1          | 2     |
| Other (porencephaly angioma cerebral atrophy etc.) | 5               | 2          | 7     |
| No pathology detected                              | 11              | 9          | 20    |
| Total  | 25              | 25         | 50    |

### Methods

**Subjects** Fifty patients were admitted to the investigation, comprising three diagnostic groups (1) spontaneous subarachnoid haemorrhage, (2) possible intracranial neoplasm, and (3) epilepsy presenting after the age of 30 years. It was correctly anticipated that in the majority of this last group no cerebral lesion would be demonstrable and these subjects therefore provided the best available substitute for 'normal controls'. The final diagnoses, after full investigation and follow up where appropriate, are shown in Table 1.

**Procedure** From routine admissions to the Department of Neurosurgery patients were selected (by A.E.B.) to form two groups which were matched with respect to five variables as shown in Table 2. One group was investigated with Hypaque and the other with Conray.

The other investigators did not know what medium had been selected. In order to assess the possible influence of technical proficiency upon the sequelae of angiography two operators of presumably differing skill were employed, the one a consultant neuroradiologist and the other a neurosurgical registrar.

General clinical assessment was carried out (by A.E.B.) on the day before angiography with particular attention to some 30 clinical features considered likely to influence the occurrence of complications.

Neurologic examinations and EEG recordings were performed serially (I) on the day before angiography, (II) 1-1 1/2 hours before commencement of angiography, (III) immediately before the patient entered the radiologic de-

## CLINICAL AND ELECTROENCEPHALOGRAPHIC SEQUELAE OF CAROTID ANGIOGRAPHY

by

C D BINNIE, D C BERNSTEIN, A E BOOTH, I R MCCAUL,  
J H MARGERISON † and J F SCOTT

Side effects of a diagnostic procedure are always a matter for concern and those of carotid angiography have been studied extensively. FIELD *et coll* (1962) found close agreement between previous reports and concluded that the incidence of complications, whether fatal or trivial, transitory or permanent, was 2 to 3%. More recent investigations suggest this level to be maintained (LINDNER & GURDJIAN 1966, KRICHIEFF & CHASE 1967). However, most investigations appear to rely on retrospective analysis of routine hospital records, and little attempt has been made to carry out detailed neurologic assessment within a few minutes of angiography in order to detect minor and transient changes

of 50 patients submitted  
to 1 on standardised serial  
neurologic examinations, reinforced by electroencephalographic investigations. Consideration was given to a large number of variables which might possibly influence the occurrence of complications and in particular two contrast media, Conray 280 (meglumine iothalamate) and Hypaque 45% (a sodium diatrizoate/meglumine diatrizoate combination), were compared

by PAMPIGLIONE (1956) Two types of record were obtained At each stage (I—VI) of the investigation a short standardised tracing was taken, following a fixed sequence of montages and of eye opening and closure At stages I (on the day before angiography) and V (2 hours after angiography) an additional record was obtained in a more routine manner, the technician being free to follow whatever procedure appeared likely to yield most information of clinical relevance These two types of tracing will be described as 'standardised' and 'routine' respectively

The EEGs were marked with code numbers and bore no other means of identification Some months after completion of data collection standardised tracings from each patient were assessed (by CDB) in random order and without any clinical information They were ranked on some 5 to 10 variables, as dominant frequency, amount of fast activity, degree of asymmetry etc These were not predetermined but were chosen as being those which most effectively discriminated between the different members of each set of 6 EEGs

After all 50 sets of standardised records had been assessed the two routine tracings of each patient were examined The identity of the patient was again concealed but the provisional diagnosis was stated The preangiographic (stage I) EEG was examined first and the abnormal features, if any, were entered on a proforma A clinical opinion was then written, including predictions where possible as to the site of any lesion The second (stage V) record was then assessed and any differences from the previous findings were entered on the form again a clinical opinion was expressed

The observations on the routine records were then compared with those on the standardised tracings The latter, having been assessed without knowledge of the order in which they were taken, provided a check against observer bias No alleged change between the first (stage I) and second (stage V) routine records was accepted as real unless the ranking of the standardised EEGs indicated a similar difference between preangiographic (stages I, II and III) and postangiographic (stages IV and V) tracings In fact, there was close agreement between the two methods of assessment Finally the clinical predictions concerning the routine tracings were compared with the definitive diagnoses and were categorised as correct, incorrect or untestable

ad

was

1 %

W and were introduced into the skin and round the common carotid artery A short bevelled thin walled 18 gauge needle was then inserted into the artery and so positioned that a free reflux of blood was obtained Saline was injected slowly to maintain patency between injections of contrast medium

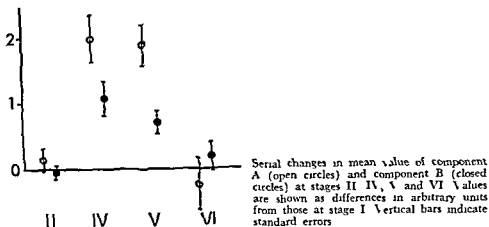
A log was kept throughout angiography, detailing the numbers of injections,

Table 2  
*Matching of Hypaque and Conray groups*

| Factors employed for preangiographic matching of groups | Contrast medium |            |       |
|---|-----------------|------------|-------|
|   | Hypaque 45 °    | Conray 280 | Total |
| Provisional diagnosis                                   |                 |            |       |
| Subarachnoid haemorrhage                                | 11              | 11         | 22    |
| Epilepsy of late onset                                  | 5               | 7          | 12    |
| Suggested tumour  | 9               | 7          | 16    |
| Awareness   |                 |            |       |
| Unimpaired  | 18              | 15         | 33    |
| Impaired, no disorientation                             | 4               | 5          | 9     |
| Impaired disorientation                                 | 3               | 5          | 8     |
| Age   |                 |            |       |
| 4th decade  | 3               | 3          | 6     |
| 5th '   | 1               | 5          | 6     |
| 6th '   | 7               | 6          | 13    |
| 7th   | 9               | 7          | 16    |
| 8th   | 5               | 4          | 9     |
| Blood pressure  |                 |            |       |
| 160/90 mm Hg  | 17              | 18         | 35    |
| Systolic > 160 mm or diastolic 90—100 mm                | 6               | 3          | 9     |
| Diastolic 100 mm  | 2               | 4          | 6     |
| Sex   |                 |            |       |
| Male  | 16              | 17         | 33    |
| Female  | 9               | 8          | 17    |
| Total   | 25              | 25         | 50    |

partment, 45 minutes after administration of premedication (EEG only neurologic examination being considered likely to arouse the patient and thus defeat the objects of premedication), (IV) immediately after completion of angiography, (V) 2 hours, and (VI) 24 hours after completion of angiography. Neurologic examination was based on a battery of standardised tests applied by a single observer experienced in their use (BINNIE 1968).

*Electroencephalography* A Kaiser Type 55 8 channel electroencephalograph was used throughout. Twenty-two chlorided silver stick on electrodes, or occasionally platinum needles, were applied in a pattern similar to that described



The initial value of component B, which related to asymmetry of neurologic signs, was appreciably higher in the subjects with cerebral haemorrhage or vascular occlusion than in the others, there being significant differences between the diagnostic groups at stage I ( $p < 0.05$ ). No significant change occurred over the pre angiographic period (stages I and II), indeed the mean value of component B fell slightly (by 14%). Over the course of angiography (stages II to IV), there was a general, significant rise in the mean value of component B ( $p < 0.01$ ), involving all diagnostic groups save the 2 patients with cerebral thrombosis. Over the two hours following angiography, component B declined more rapidly than did component A, but remained significantly higher than at stage I or II ( $p < 0.001$ ). By stage VI (24 hours after angiography), component B had virtually returned to its initial level (cf. the Figure). The changes which gave rise to these alterations in mean values of component B were shown by 26 patients. Increase in component B was slightly commoner among subjects without demonstrable lesions (65%) than in the total sample (52%), and rarer in those with ruptured aneurysms (38%).

In summary, physical state was stable before angiography but deteriorated between premedication and completion of the angiography, with respect both to state of awareness (in 66% of patients) and to hemisyndromes (in 52%). There was some improvement over the following 2 hours, with full recovery by 24 hours. The patients without demonstrable lesions appeared particularly vulnerable but this may simply indicate that it was easier to detect slight deterioration in subjects who were previously normal.



amounts of contrast medium, duration of carotid compression etc To assess the technical difficulty and trauma of each carotid puncture four indices were used (1) the operator's subjective evaluation of the difficulty on a 5 point scale, (2) the time taken from penetration of the skin to the obtaining of a satisfactory reflux of blood, (3) the number of thrusts required before the needle satisfactorily punctured the artery and (4) the operator's assessment of the mobility of the artery on a 3 point scale

*Assessment of discomfort* After each injection and at stages V and VI, the patients were asked standardised questions (by CDB) concerning their experiences

*Evaluation of angiograms* The quality of contrast obtained in all 50 sets of angiograms was assessed at a single session (by DCB), the films being categorised as good, fair or poor

## Results

*Neurologic observations* The neurologic data for each patient amounted to 5 sets of observations on 38 different variables In order to obtain some simple measure of clinical change, these results were subjected to principal component analysis (see Appendix) Two factors appeared at all stages of the investigation and accounted for some 30 % of the total population variance The first, component A, was a general index of drowsiness and of unresponsiveness to stimulation The other, component B, related to hemisyndromes, asymmetries of tone, of power or of sensation, sensory inattention etc Before angiography (stages I and II) there were significant differences ( $p < 0.05$ ) between the mean values of component A in each of the definitive diagnostic groups, due to a low mean value in patients without detectable pathology

Between stages I and II there was no significant change of component A either in the total sample or in subgroups, thus the component was stable before angiography Immediately after angiography and two hours later (stages IV and V) the mean value of component A was significantly elevated above its initial value ( $p < 0.001$  at both stages) At stage VI (24 hours after angiography) it had returned to its original level (cf the Figure) However, not all patients showed this deterioration of awareness and responsiveness after angiography, an increase of component A from stage II to stage IV was seen in only 33 subjects There were no significant differences between the diagnostic groups, and elevation of component A occurred in approximately the same proportion of the patients without demonstrable pathology (70 %) as of the total sample (66 %)

Table 4

*Postangiographic changes in the EEG classified by diagnosis*

| EEG findings                     | SAH<br>aneurysm | SAH<br>other<br>lesion | Cereb<br>haem | Tumours | Cereb<br>thrombosis | Other | No<br>demon-<br>strable<br>pathology | Total |
|----------------------------------|-----------------|------------------------|---------------|---------|---------------------|-------|--------------------------------------|-------|
| <i>Post-central</i>              |                 |                        |               |         |                     |       |                                      |       |
| <i>dominant frequency</i>        |                 |                        |               |         |                     |       |                                      |       |
| Increased                        | 4               | 0                      | 0             | 1       | 0                   | 1     | 5                                    | 11    |
| Unchanged                        | 4               | 0                      | 0             | 1       | 2                   | 3     | 8                                    | 18    |
| Decreased                        | 5               | 1                      | 2             | 4       | 0                   | 2     | 7                                    | 21    |
| <i>Background asymmetry</i>      |                 |                        |               |         |                     |       |                                      |       |
| Decreased                        | 3               | 0                      | 2             | 0       | 0                   | 0     | 4                                    | 9     |
| Unchanged                        | 6               | 1                      | 0             | 2       | 1                   | 4     | 13                                   | 27    |
| Increased                        | 4               | 0                      | 0             | 4       | 1                   | 2     | 3                                    | 14    |
| <i>Other diffuse abnormality</i> |                 |                        |               |         |                     |       |                                      |       |
| Decreased                        | 4               | 1                      | 1             | 0       | 0                   | 1     | 3                                    | 10    |
| Unchanged                        | 2               | 0                      | 0             | 4       | 1                   | 3     | 13                                   | 23    |
| Increased                        | 7               | 0                      | 1             | 2       | 1                   | 2     | 4                                    | 17    |
| <i>Local abnormality</i>         |                 |                        |               |         |                     |       |                                      |       |
| Decreased                        | 0               | 0                      | 1             | 0       | 1                   | 3     | 6                                    | 11    |
| Unchanged                        | 7               | 1                      | 0             | 0       | 1                   | 2     | 10                                   | 21    |
| Increased                        | 5               | 0                      | 0             | 1       | 0                   | 0     | 3                                    | 9     |
| Different site                   | 1               | 0                      | 1             | 5       | 0                   | 0     | 1                                    | 8     |
| Different nature                 | 0               | 0                      | 0             | 0       | 0                   | 1     | 0                                    | 1     |
| <i>Peroxyimal activity</i>       |                 |                        |               |         |                     |       |                                      |       |
| Decreased                        | 2               | 0                      | 0             | 0       | 1                   | 0     | 3                                    | 6     |
| Unchanged                        | 9               | 1                      | 2             | 6       | 1                   | 5     | 15                                   | 39    |
| Increased                        | 2               | 0                      | 0             | 0       | 0                   | 1     | 2                                    | 5     |
| Total in<br>Diagnostic group     | 13              | 1                      | 2             | 6       | 2                   | 6     | 20                                   |       |

*Electroencephalographic observations*

*Initial findings* The EEG observations before angiography (routine record, stage I) are summarised in Table 3. The diagnostic groups differed significantly with respect to post-central dominant frequency ( $p < 0.05$ ), diffuse abnormalities ( $p < 0.01$ ), and local abnormalities ( $p < 0.001$ ). There was an excess of diffuse abnormalities in patients with tumours or intracranial bleeding, and

Table 3

*Initial EEG findings classified by diagnosis*

| EEG findings                     | SAH<br>aneurysm | SAH<br>other<br>lesion | Cereb<br>haem | Tumours | Cereb<br>thrombosis | Other | No<br>demon-<br>strable<br>pathology | Total |
|----------------------------------|-----------------|------------------------|---------------|---------|---------------------|-------|--------------------------------------|-------|
| <i>Post central</i>              |                 |                        |               |         |                     |       |                                      |       |
| <i>domin frequency</i>           |                 |                        |               |         |                     |       |                                      |       |
| 9 c/s or more                    | 4               | 1                      | 2             | 4       | 0                   | 4     | 15                                   | 30    |
| 8-8 1/2 c/s                      | 6               | 0                      | 0             | 1       | 1                   | 2     | 4                                    | 14    |
| 8 c/s or less                    | 3               | 0                      | 0             | 1       | 1                   | 0     | 1                                    | 6     |
| <i>Background asymmetry</i>      |                 |                        |               |         |                     |       |                                      |       |
| Nil/normal                       | 2               | 0                      | 0             | 1       | 1                   | 1     | 6                                    | 11    |
| Minor                            | 9               | 1                      | 1             | 4       | 1                   | 4     | 11                                   | 31    |
| Marked                           | 2               | 0                      | 1             | 1       | 0                   | 1     | 3                                    | 8     |
| <i>Other diffuse abnormality</i> |                 |                        |               |         |                     |       |                                      |       |
| Nil                              | 3               | 0                      | 0             | 0       | 0                   | 1     | 10                                   | 14    |
| Uncertain                        | 2               | 0                      | 0             | 1       | 2                   | 1     | 7                                    | 13    |
| Clear                            | 8               | 1                      | 2             | 5       | 0                   | 4     | 3                                    | 23    |
| <i>Local abnormality</i>         |                 |                        |               |         |                     |       |                                      |       |
| Nil                              | 7               | 1                      | 0             | 0       | 0                   | 2     | 11                                   | 21    |
| Uncertain                        | 4               | 0                      | 0             | 0       | 0                   | 3     | 4                                    | 11    |
| Clear                            | 2               | 0                      | 2             | 6       | 2                   | 1     | 5                                    | 18    |
| <i>Local delta activity</i>      |                 |                        |               |         |                     |       |                                      |       |
| Nil                              | 10              | 1                      | 0             | 0       | 1                   | 3     | 16                                   | 31    |
| Present                          | 3               | 0                      | 2             | 6       | 1                   | 3     | 4                                    | 19    |
| <i>Local paroxysmal activity</i> |                 |                        |               |         |                     |       |                                      |       |
| Nil                              | 11              | 1                      | 2             | 6       | 1                   | 4     | 15                                   | 40    |
| Present                          | 2               | 0                      | 0             | 0       | 1                   | 2     | 5                                    | 10    |
| <i>Other paroxysmal activity</i> |                 |                        |               |         |                     |       |                                      |       |
| Nil                              | 11              | 1                      | 2             | 6       | 2                   | 5     | 19                                   | 46    |
| Uncertain                        | 2               | 0                      | 0             | 0       | 0                   | 1     | 0                                    | 3     |
| Clear                            | 0               | 0                      | 0             | 0       | 0                   | 0     | 1                                    | 1     |
| Total in diagnostic group        | 13              | 1                      | 2             | 6       | 2                   | 6     | 20                                   |       |

Table 4

*Postangiographic changes in the EEG classified by diagnosis*

| EEG findings                     | SAH<br>aneurysm | SAH<br>other<br>lesion | Cereb<br>haent | Tumours | Cereb<br>thrombosis | Other | No<br>demon<br>strable<br>pathology | Total |
|----------------------------------|-----------------|------------------------|----------------|---------|---------------------|-------|-------------------------------------|-------|
| <i>Post-central</i>              |                 |                        |                |         |                     |       |                                     |       |
| <i>dominant frequency</i>        |                 |                        |                |         |                     |       |                                     |       |
| Increased                        | 4               | 0                      | 0              | 1       | 0                   | 1     | 5                                   | 11    |
| Unchanged                        | 4               | 0                      | 0              | 1       | 2                   | 3     | 8                                   | 18    |
| Decreased                        | 5               | 1                      | 2              | 4       | 0                   | 2     | 7                                   | 21    |
| <i>Background asymmetry</i>      |                 |                        |                |         |                     |       |                                     |       |
| Decreased                        | 3               | 0                      | 2              | 0       | 0                   | 0     | 4                                   | 9     |
| Unchanged                        | 6               | 1                      | 0              | 2       | 1                   | 4     | 13                                  | 27    |
| Increased                        | 4               | 0                      | 0              | 4       | 1                   | 2     | 3                                   | 14    |
| <i>Other diffuse abnormality</i> |                 |                        |                |         |                     |       |                                     |       |
| Decreased                        | 4               | 1                      | 1              | 0       | 0                   | 1     | 3                                   | 10    |
| Unchanged                        | 2               | 0                      | 0              | 4       | 1                   | 3     | 13                                  | 23    |
| Increased                        | 7               | 0                      | 1              | 2       | 1                   | 2     | 4                                   | 17    |
| <i>Local abnormality</i>         |                 |                        |                |         |                     |       |                                     |       |
| Decreased                        | 0               | 0                      | 1              | 0       | 1                   | 3     | 6                                   | 11    |
| Unchanged                        | 7               | 1                      | 0              | 0       | 1                   | 2     | 10                                  | 21    |
| Increased                        | 3               | 0                      | 0              | 1       | 0                   | 0     | 3                                   | 9     |
| Different site                   | 1               | 0                      | 1              | 5       | 0                   | 0     | 1                                   | 8     |
| Different nature                 | 0               | 0                      | 0              | 0       | 0                   | 1     | 0                                   | 1     |
| <i>Paroxysmal activity</i>       |                 |                        |                |         |                     |       |                                     |       |
| Decreased                        | 2               | 0                      | 0              | 0       | 1                   | 0     | 3                                   | 6     |
| Unchanged                        | 9               | 1                      | 2              | 6       | 1                   | 5     | 15                                  | 39    |
| Increased                        | 2               | 0                      | 0              | 0       | 0                   | 1     | 2                                   | 5     |
| Total in<br>Diagnostic group     | 14              | 1                      | 2              | 6       | 2                   | 6     | 20                                  |       |

*Electroencephalographic observations*

*Initial findings* The EEG observations before angiography (routine record, stage I) are summarised in Table 3. The diagnostic groups differed significantly with respect to post-central dominant frequency ( $p < 0.05$ ), diffuse abnormalities ( $p < 0.01$ ), and local abnormalities ( $p < 0.001$ ). There was an excess of diffuse abnormalities in patients with tumours or intracranial bleeding, and

Table 3

*Initial EEG findings classified by diagnosis*

| EEG findings                     | SAH<br>aneurysm | SAH<br>other<br>lesion | Cereb.<br>haem. | Tumours | Cereb<br>thrombosis | Other | No<br>demon-<br>strable<br>pathology | Total |
|----------------------------------|-----------------|------------------------|-----------------|---------|---------------------|-------|--------------------------------------|-------|
| <i>Post central</i>              |                 |                        |                 |         |                     |       |                                      |       |
| <i>domin. frequency</i>          |                 |                        |                 |         |                     |       |                                      |       |
| 9 c/s or more                    | 4               | 1                      | 2               | 4       | 0                   | 4     | 15                                   | 30    |
| 8-8 1/2 c/s                      | 6               | 0                      | 0               | 1       | 1                   | 2     | 4                                    | 14    |
| 8 c/s or less                    | 3               | 0                      | 0               | 1       | 1                   | 0     | 1                                    | 6     |
| <i>Background asymmetry</i>      |                 |                        |                 |         |                     |       |                                      |       |
| Nil/normal                       | 2               | 0                      | 0               | 1       | 1                   | 1     | 6                                    | 11    |
| Minor                            | 9               | 1                      | 1               | 4       | 1                   | 4     | 11                                   | 31    |
| Marked                           | 2               | 0                      | 1               | 1       | 0                   | 1     | 3                                    | 8     |
| <i>Other diffuse abnormality</i> |                 |                        |                 |         |                     |       |                                      |       |
| Nil                              | 3               | 0                      | 0               | 0       | 0                   | 1     | 10                                   | 14    |
| Uncertain                        | 2               | 0                      | 0               | 1       | 2                   | 1     | 7                                    | 13    |
| Clear                            | 8               | 1                      | 2               | 5       | 0                   | 4     | 3                                    | 23    |
| <i>Local abnormality</i>         |                 |                        |                 |         |                     |       |                                      |       |
| Nil                              | 7               | 1                      | 0               | 0       | 0                   | 2     | 11                                   | 21    |
| Uncertain                        | 4               | 0                      | 0               | 0       | 0                   | 3     | 4                                    | 11    |
| Clear                            | 2               | 0                      | 2               | 6       | 2                   | 1     | 5                                    | 18    |
| <i>Local delta activity</i>      |                 |                        |                 |         |                     |       |                                      |       |
| Nil                              | 10              | 1                      | 0               | 0       | 1                   | 3     | 16                                   | 31    |
| Present                          | 3               | 0                      | 2               | 6       | 1                   | 3     | 4                                    | 19    |
| <i>Local paroxysmal activity</i> |                 |                        |                 |         |                     |       |                                      |       |
| Nil                              | 11              | 1                      | 2               | 6       | 1                   | 4     | 15                                   | 40    |
| Present                          | 2               | 0                      | 0               | 0       | 1                   | 2     | 5                                    | 10    |
| <i>Other paroxysmal activity</i> |                 |                        |                 |         |                     |       |                                      |       |
| Nil                              | 11              | 1                      | 2               | 6       | 2                   | 5     | 19                                   | 46    |
| Uncertain                        | 2               | 0                      | 0               | 0       | 0                   | 1     | 0                                    | 3     |
| Clear                            | 0               | 0                      | 0               | 0       | 0                   | 0     | 1                                    | 1     |
| Total in diagnostic group        | 13              | 1                      | 2               | 6       | 2                   | 6     | 20                                   |       |

Table 6

*Neurological and EEG changes after angiography with Hypaque or Conray*

|   | Contrast medium |        |
|---|-----------------|--------|
|   | Hypaque         | Conray |
| Neurological factors (mean values in arbitrary units) |                 |        |
| Change in A stage II to IV                            | +2.4            | +1.6   |
| Change in B stage II to IV                            | +1.3            | +0.8   |
| Change in A stage II to V                             | +2.2            | +1.5   |
| Change in B stage II to V                             | -1.2            | +0.2   |
| EEG changes (number of patients)                      |                 |        |
| Post-central dominant frequency                       |                 |        |
| Increased   | 4               | 7      |
| Decreased   | 12              | 9      |
| Background asymmetry                                  |                 |        |
| Decreased   | 3               | 6      |
| Increased   | 8               | 6      |
| Diffuse abnormalities                                 |                 |        |
| Decreased   | 5               | 5      |
| Increased   | 10              | 7      |
| Local abnormality                                     |                 |        |
| Decreased   | 4               | 7      |
| Increased   | 6               | 3      |
| Paroxysmal activity                                   |                 |        |
| Decreased   | 1               | 5      |
| Increased   | 3               | 2      |

*Comparison of contrast media* Matching of the patients investigated with Conray to those receiving Hypaque was satisfactory (Tables 1 and 2). The two groups were also similar with respect to the neurologic components: number of

components A and B from stage II to IV were 2.4 and 1.3 with Hypaque and slightly less, 1.6 and 0.8 with Conray. However, by stage V (2 hours after angiography), component B had fallen to within 0.2 of its original value in the Conray group but remained elevated by 1.2 in subjects receiving Hypaque, a significant difference in favour of Conray ( $p < 0.05$ ) (Table 6). No significant differences in incidence of EEG changes

Table 5

*Initial neurological and EEG abnormalities in Hypaque and Conray groups*

|   | Contrast medium |          |
|---|-----------------|----------|
|   | Hypaque         | Conray   |
| Neurologic factors (mean values in arbitrary units) |                 |          |
| A   | 19.8            | 21.2     |
| B   | 0.2             | 0.6      |
| EEG abnormalities (number of patients)              |                 |          |
| Post central dominant below 8 c/s                   | 3               | 3        |
| Background asymmetry, minor or major                | 21              | 18       |
| Local Delta activity                                | 8               | 11       |
| Clear, diffuse abnormality                          | 10              | 13       |
| Local paroxysmal activity                           | 4               | 6        |
| Number of injections (mean values)                  | 3.19            | 3.24     |
| Dosage of contrast                                  | 23.21 ml        | 23.39 ml |

local slow activity occurred in all those with tumours or primary intracerebral haemorrhage. In subjects without demonstrable pathology, gross EEG disturbances were uncommon but in less than a third were the tracings normal.

*Post-angiographic findings* Changes in the routine records after angiography (stage V) showed no constant pattern but the general trend was towards the development or worsening of abnormalities (Table 4). Thus the post-central dominant frequency fell in 21 subjects but rose in only 11, asymmetries of background activity increased in 14 but became less in 9, diffuse abnormalities were accentuated in 17 and diminished in 10. Localised abnormalities changed in nearly three fifths of the patients. In 9 the disturbance was simply increased but in 8 — including 5 of the 6 subjects with tumors — its distribution was altered, in 11 the abnormality was less marked. A total of 38 patients (76%) showed some increase of EEG abnormalities.

*Diagnostic predictions* From the preangiographic EEGs, 17 lesions were correctly localised and 6 incorrect predictions were made. After angiography there were only 15 correct statements and the number of errors was unchanged. Four aneurysms were wrongly localised before angiography but 3 of the errors were corrected when the postangiographic tracing was seen. By contrast, no tumours were wrongly located before angiography but the postangiographic record led to incorrect localisation in 3 (50%).

impairment of awareness (component A) in 66 % of the subjects may be attributable to premedication. The increase in hemisyndromes (component B) is less readily explained in this way: the components were so defined as to be nearly uncorrelated (see Appendix), the increase in asymmetrical signs (component B) is not therefore due simply to drowsiness, (component A).

As the degree of sedation probably influences the difficulty of carotid puncture, it was reluctantly decided that to disturb the patient by neurologic examination immediately before angiography and after premedication (stage III) was not permissible. Nevertheless an EEG was obtained at this point and it will be recalled that the EEG changes reported include only those which distinguished the postangiographic tracings from all preangiographic records (including stage III). Thus the EEG observations confirm that there was widespread alteration of cerebral function over the period of angiography. An attempt has been made to monitor the EEG during angiography in 25 patients (WHITEHEAD *et coll* 1966). Some patients showed marked deterioration of the tracing or developed new abnormalities a few seconds after injections of contrast medium. However, the picture was so complicated by the effects of fluctuations in state of awareness that no reliable quantitative interpretation seemed possible (BINNIE & MARGERISOV 1966). Such difficulties are not mentioned by LUNDVOLD & ENGESET (1966) who found EEG changes in up to 21 % of subjects, depending upon the technique and contrast medium employed.

The incidence of serious complications of angiography is reported to be highest in elderly arteriosclerotic patients and in those with ruptured intracranial aneurysms or tumours (DUNSMORE *et coll* 1951, LINDNER *et coll* 1962, TORMA & FÖGELHOLM 1967). By contrast, the comparatively trivial and transient neurologic changes described above were least marked in the older subjects and in those with a history of cerebrovascular accident. This paradox may reflect different mechanisms underlying the minor sequelae and the major complications

thrombosis at the site

major complica

transient changes

may be due to alteration in cerebrovascular tone, for contrast media are variously reported as causing cerebral vaso-constriction (INGVAR & SÖDERBERG 1957), dilatation and endothelial damage (KÄGSTROM *et coll* 1960, BLOOR *et coll* 1951) or combinations of constriction and dilatation (FOLTZ *et coll* 1952). It might be expected that sclerotic vessels would be less influenced by agents affecting vascular tone at an arteriolar level, while if the action on capillaries was predominately dilator, cerebral perfusion could even be improved. It is therefore of interest that some of the oldest patients in the series were considerably more alert 24 hours after angiography than they had been before investigation.



were found between the two groups although there was a trend in favour of Conray (Table 6)

To permit comparison of the media with respect to the subjective experience of the patients, the observations on reports of discomfort were treated by principle component analysis and two components extracted. The first of these (C) related to total discomfort, the second (D) to a comparison between immediate distress and complaints on the day after angiography. There were no significant differences between the two groups of patients, but again a slight advantage lay with Conray, which gave smaller scores on both components.

A comparative evaluation of the technical performance of the two contrast media was not attempted, but the crude assessment of the quality of the films indicates that the media were used in such concentrations and dosage as to yield similar results. It is therefore reasonable to draw comparisons between the side-effects which occurred under the conditions of this investigation.

In summary, the differences found between the contrast media were slight and rarely of statistical significance. Nevertheless, adverse effects were consistently less when Conray was used.

*Other factors which may influence clinical and EEG changes.* Neither the number of injections, the total dose of contrast medium, nor the difficulty of inserting the needle had any apparent influence on the occurrence of neurologic or EEG changes. These variables were, however, the main factors determining the discomfort reported by the patient (significant correlations with component C,  $p < 0.05$  or  $< 0.01$ ).

The older subjects tolerated angiography better than might be expected. Age showed significant negative correlations with deterioration of awareness after angiography (as measured by elevation of component A between stages II and V,  $p < 0.05$ ) and with increase in severity and incidence of hemisyndromes (change of component B stage II to stages IV and V,  $p < 0.05$  and  $< 0.01$  respectively). Less discomfort was reported by the older patients due possibly to the greater ease of carotid puncture (negative correlations of age with discomfort, and with component C,  $p < 0.05$ , and with difficulty of puncture  $p < 0.01$ ).

### Discussion

By the criteria apparently employed in most previous investigations no neurologic complications occurred in this series of 50 angiographic examinations and, as the generally reported incidence is 2% to 3%, the results compare not unfavourably with those obtained elsewhere. It is nevertheless of more than passing interest that a detailed search for transient neurologic change revealed widespread, if reversible, deterioration within the 2 hours after angiography. The

### Acknowledgements

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### SUMMARY

Serial neurologic and EEG examinations of 50 patients before and after carotid angiography revealed no major complications but minor neurologic deterioration was detected in over half the patients. The changes tended to be less when Conray was used than with Hypaque, although the differences between the two were rarely significant. EEG abnormalities increased over the period of angiography and, although post angiographic EEGs were valuable for localisation of ruptured intracranial aneurysms, in patients with cerebral tumours EEGs taken two hours after angiography were liable to lead to incorrect localisation.

### ZUSAMMENFASSUNG

Neurologische und EEG Serien Untersuchungen von 50 Patienten vor und nach einer Carotis Angiographie ergaben keine grosseren Komplikationen, während geringere neurologische Störungen in über der Hälfte der Patienten gefunden wurden. Diese Veränderungen waren etwas geringer bei der Verwendung von Conray gegenüber derjenigen von Hypaque, obwohl die Unterschiede zwischen diesen beiden kaum signifikant waren. EEG Anomalien waren häufiger während der Periode der Angiographie und, obwohl postangiographische EEGs zur Lokalisation eines rupturierten intracranialen Aneurysmas von Wert waren, konnten EEGs bei Patienten mit cerebralen Tumoren zwei Stunden nach der Angiographie zu einer falschen Lokalisation führen.

### RÉSUMÉ

Des examens neurologiques et electro-encephalographiques en serie de 50 malades avant et apres angiographie carotidienne n'ont pas montre de complication majeure mais ont montre, dans plus de la moitié des cas, une aggravation neurologique mineure.

Les EEG enregistrés deux heures après l'angiographie pouvaient causer une erreur de localisation dans les cas de tumeur cérébrale.

Only minor differences were found between the two contrast media, yet in every respect a slight advantage lay with Conray. These findings may be compared with those of KRICHIEFF & CHASE (1967) who also found only marginal differences between meglumine diatrizoate and iothalamate. It would be unwise to draw any firm conclusion concerning the relative merits of these two media, but on present evidence Conray is to be preferred.

Clinical neurophysiologists are often asked to perform EEG investigations on a patient who has already undergone angiography. It has been shown elsewhere (BINNIE 1968, BINNIE et coll. 1969) that for purposes of localising ruptured intracranial aneurysms EEGs taken 2 hours after angiography are of particular value. The findings in the present small sample of patients with aneurysms are in accordance with that view. However, the postangiographic records proved misleading for the location of tumours. The present investigation does not indicate the duration of the EEG disturbances following angiography, but suggests that where the diagnosis of cerebral tumour is in question EEGs taken immediately after angiography should be interpreted with the greatest caution and if possible repeated at some later date.

### Appendix

*Component analysis* is a method for reducing the dimensions of a large number of interrelated variables. Consider  $p$  variables  $x_1, x_2, x_3, \dots, x_p$  each observed on  $n$  individuals. The variables  $x$  are transformed to a new set of variables  $z_1, z_2, \dots, z_p$  called the principal components, by a linear transformation of the type

$$z_i = \sum_{j=1}^p a_{ij} x_j \quad i=1, 2, \dots, p$$

The coefficients  $a_{ij}$ , which are called the loadings must satisfy the two conditions (1) that the new variables  $z$  should be uncorrelated (and therefore can be considered separately) and (2) that the first component  $z_1$  should have as large a variance as possible, the second should account for as large a proportion as possible of the remaining variability subject to condition (1) and so on.

It is often possible to account for a large part of the variation in the original data by only a few components. If the original pattern of variation is stable, then the same, or nearly the same, components should appear on repeated occasions of measurement, but slight fluctuations in the pattern of variation may cause the components to occur in a different order, or to be somewhat modified. The percentage of variation accounted for by each component is a measure of its importance.

For purposes of calculating the components the loadings were converted to whole numbers for simplicity, and so may not be exactly uncorrelated. They should nevertheless summarise the most important sources of variation in the original data. Numerical values for components A—D were calculated for each patient and compared with other variables. Correlations were calculated as product moments and the significance levels cited in the text were determined by Student's  $t$  test.

## TRANSVERSE TOMOGRAPHY WITH MIMER III

by

K. BERGSTROM, L. HOLMSTROM, H. LODIN, O. NILÉN and H. WILBRAND

Tomography has become increasingly necessary in neuro- and otoradiology so that modern equipment is nearly always supplied with a tomographic device. One example of such a unit is the Mimer, and its latest version, Mimer III, is suspended from the ceiling (FREDZELL et coll 1968, CROONQVIST 1969). Only linear tomography can be performed although this is usually considered adequate for routine examinations and scientific purposes.

Some authors, e.g. SANSONE et coll (1951), TAKAHASHI et coll (1952, 1969), DI CHIRO (1964, 1965) have, however, also described the use of transverse tomography in neuroradiologic examinations. SANSONE et coll. and DI CHIRO employed this technique in encephalography, and TAKAHASHI both in encephalography and skull examinations. SANSONE et coll. used a Pantux Strator Zuder, and DI CHIRO a Philips Radiotome, with which the seated patient and the cassette rotated during the exposure, while the tube was stationary. TAKAHASHI employed the Toshiba tomographic equipment, with which the patient was examined supine and lay still during the exposure while the roentgen tube and cassette rotated. There appear to be no reports on the use of transverse tomography in special otoradiologic examinations.

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## TRANSVERSE TOMOGRAPHY WITH MIMER III

by

K BERGSTROM, L HOLMSTROM, H LODIN, O NYLEN and H WILBRAND

Tomography has become increasingly necessary in neuro- and otoradiology so that modern equipment is nearly always supplied with a tomographic device. One example of such a unit is the Mimer, and its latest version, Mimer III, is suspended from the ceiling (FREDZELL et coll 1968, CRONQVIST 1969). Only linear tomography can be performed although this is usually considered adequate for routine examinations and scientific purposes.

Some authors, e.g. SANSONE et coll (1951), TAKAHASHI et coll (1952, 1969), DI CHIRO (1964, 1965) have, however, also described the use of transverse tomography in neuroradiologic examinations. SANSONE et coll and DI CHIRO employed this technique in encephalography, and TAKAHASHI both in encephalography and skull examinations. SANSONE et coll used a Pantux Strator Zuder, and DI CHIRO a Philips Radiotome, with which the seated patient and the cassette rotated during the exposure, while the tube was stationary. TAKAHASHI employed the Toshiba tomographic equipment, with which the patient was examined supine and lay still during the exposure while the roentgen tube and cassette rotated. There appear to be no reports on the use of transverse tomography in special otoradiologic examinations.

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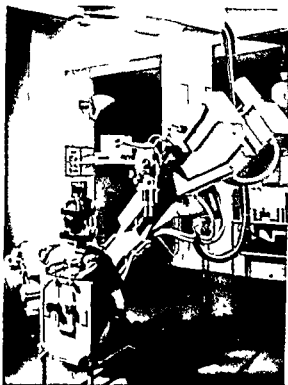


Fig 1

Fig 1 Mimer III arranged for transverse tomography. The tomographic equipment is mounted in place of the routine cassette holder. The patient with the head fixed sits in a special chair.

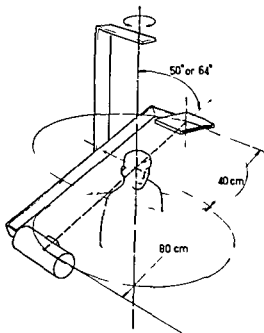


Fig 2

As it was considered that transverse tomography may be an interesting and valuable complement to linear tomography in certain examinations, the Mimer III of the authors has been equipped with a special tomographic unit constructed by Elema-Schonander as a prototype. The aim of this paper is to give a technical description of the unit and to present the results of some technical and clinical tests. The results of determinations of the radiation dose to the lenses of the eye and the gonads are also presented.

**Technical description.** Mimer III, mounted on the ceiling, is able to rotate around a central axis and thus fulfil a basic prerequisite for transverse tomography. Fig 1 illustrates the apparatus ready for transverse tomography with the special unit attached by means of a bolt and three control pegs. The routine cassette holder is removed and the amplifier is turned  $180^\circ$  before the unit is mounted in position. Two positions for the tube arm (Fig 2) produce a tomographic angle of either  $50^\circ$  or  $64^\circ$  (these are often given in the literature as the complement angles  $40^\circ$  and  $26^\circ$ ). The relative rotation between the stand and the cassette is electrically synchronized. The patient sits on a specially constructed chair with an arrangement for fixation of the head. The rotation chair

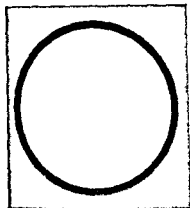


Fig 3 Pinhole test indicating the tube travel

RCT 2 (FREDZELL et coll 1968) may also be used, but only at a tomographic angle of  $64^\circ$ , since with the tube arm set at an angle of  $50^\circ$  contact takes place between the rotation chair and the circularly rotating tube during the exposure. The examination is thus confined to the larger tomographic angle in encephalography which is to be carried out with the patient fixed in the rotation chair. This system allows transverse tomography only in the horizontal plane. Special bevelled elliptical cones are provided for each of the angles. The object is positioned in the vertical central axis of the system with the aid of an illuminated cross located in this axis, the level desired for the tomograms being set by means of an indicator light located on the tube arm. The height of the tube arm can be regulated by telescopic movement of the components in the vertical arm. The angle of rotation during exposure is  $360^\circ$  and the exposure time 6 seconds. The focus-object distance is 80 cm and the object-film distance 40 cm, giving a magnification factor of 1.5. The use of a cone as a complement to the Rurek collimator is highly effective in eliminating secondary radiation. Grids may be omitted because of the 40 cm object-film distance. The focal spot size is 0.6 mm and the cassette dimensions are 18 cm  $\times$  24 cm or 24 cm  $\times$  30 cm.

A diagrammatic sketch of the system is reproduced in Fig 2. The tube and the cassette rotate during the exposure. This is an advantage compared with older forms of tomographs for examination of the sitting patient, in which the patient and the cassette rotated. Apart from the possibility that such rotation may cause discomfort to the patient, the latter system also involves a greater risk of unsharpness due to movement.

*Technical tests* These comprised the transverse, and not the linear system of Mimer III. The Mimer system was tested in its original form, with linear and circular tomography, by LINDGREN & MATTSOON (1965). The tube voltage was always 40 kV. The Agfa Gevaert RP films were developed in a 90-second auto-



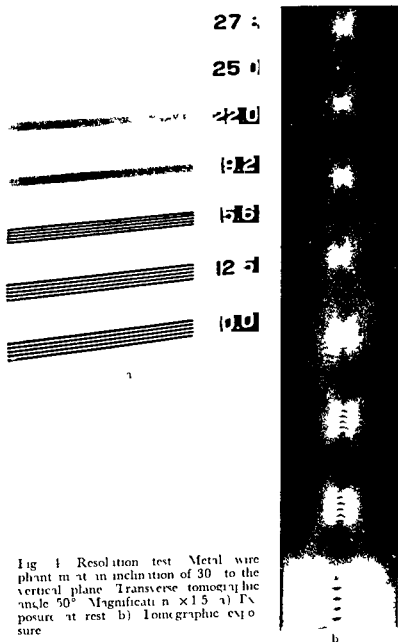


Fig. 1. Resolution test. Metal wire phantom in an inclination of 30° to the vertical plane. Transverse tomographic angle 50°. Magnification  $\times 15$ . a) Exposure at rest. b) Tomographic exposure.

matic processing unit. The cassettes were of the Siemens type with normal intensifying screens (Saphir) and mounted with lead foil against back scattering radiation; no grids were used. The pinhole test (Fig. 3) indicated the tube pathway in the form of a homogeneous circle with no irregularities. The test was carried out with a pinhole plate at the object level with projection of the central beam onto a cassette placed at a short distance below this level. It revealed that the system had good functional stability and homogeneity of exposure.

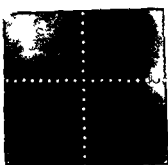


Fig 5

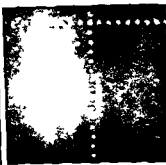


Fig 6 a

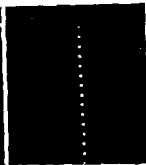


Fig 6 b

Fig 5 Phantom of metal balls (0.79 mm diameter) arranged in the form of a cross in a plane parallel to the film demonstrating the homogeneity of the tomographic plane and the mechanical stability.

Fig 6 Layer thickness demonstrated by the metal ball phantom adjusted to an inclination of  $2^\circ$  to the horizontal plane. a) Tomographic angle  $50^\circ$  b) Tomographic angle  $64^\circ$ .

The resolution was investigated with a metal wire phantom (Fig 4) with an inclination of  $30^\circ$  from the vertical plane with a tomographic angle of  $50^\circ$ . Fig 4 a gives the result of the resolution test by means of a metal wire phantom at rest and Fig 4 b the result after transverse tomographic movement. A period number of 2.5 to 2.78 can be identified, thus proving that the transverse tomographic system possesses good resolution power.

A test of mechanical stability was performed with a plexiglas plate in which metal balls, 0.79 mm in diameter and with a distance of 0.5 cm between each, were arranged in a cross pattern in one plane. Tomography at an angle of  $50^\circ$  produced uniform good reproduction of all balls, even those at a relatively considerable distance from the centre (Fig 5). The 'layer thickness' was demonstrated both with the foregoing test plate inclined  $2^\circ$  from the horizontal plane (the film plane) (Fig 6) and with a spiral wire phantom (Fig 7). About 10 balls were visible in the layer with an angle of  $50^\circ$  and about 5 balls with an angle of  $64^\circ$  (Fig 6). The spiral wire phantom was tomographed at half the height of the cylinder. The ascent of the wire was 2.5 mm per revolution, at a tomographic angle of  $50^\circ$  about a third of a revolution was demonstrated, and when the angle was increased to  $64^\circ$  only a very short segment of the wire was sharply defined. The layer was thus very thin. The 'layer thickness' may be calculated if the ends of the sharply delineated arch are connected to the axis of the cylinder (STIEVE 1968).

The tests indicate that the system possesses good stability and good resolution. Detail, however, is adversely affected by the use of double coated films and double intensifying screens.



Fig 7 Spiral wire phantom with an ascent of 2.5 mm in  $360^\circ$  demonstrating the layer thickness a) Tomographic angle  $50^\circ$  b) Tomographic angle  $64^\circ$

*Clinical tests* The time required to prepare the apparatus for transverse tomography is about 5 minutes. As with all types of tomography it is obviously important to achieve stable and effective fixation of the head of the patient. Its displacement cranio-caudally is, however, more harmful for the result in transverse than in linear tomography.

Some examples of clinical tests will be given. The tube voltage was between 60 and 70 kV. The other data were the same as in the technical tests. Better results were obtained without than with a grid, so that it was always omitted. A tomographic angle of  $50^\circ$  was used in all skeletal examinations in order to obtain the best possible contrast differences. An angle of  $64^\circ$  had to be used, as mentioned above, so as to avoid contact between the roentgen tube and the chair for encephalography performed with the patient in the rotation chair RCT-2, however.

An example of tomography of the base of the skull is presented in Fig 8, depicting a destruction in the clivus. The detail reproduction is good and delicate structures may be distinguished.

Tomograms from a normal encephalography in Fig 9 exemplify different ventricular and subarachnoid, supratentorial structures.

Further fine details are evident in the temporal bone in the form of labyrinthine and cochlear structures as well as the facial nerve canal in addition to those of the auditory ossicles in Fig 10. A large operation defect in the mastoid cells and external auditory meatus in a case of radical mastoidectomy is present.

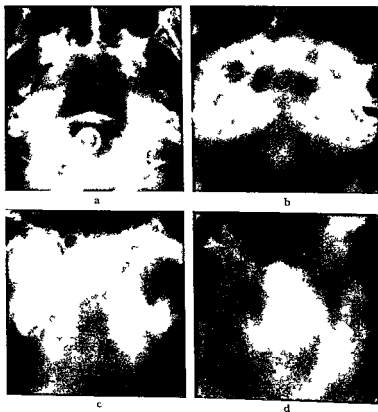


Fig 8 Destruction in region of clivus probably due to chordoma a) Conventional film Selected tomograms b) at level of petrosal bone demonstrating destruction of clivus and petrosal apices c) 1.25 cm above tomogram (b) and d) 2.25 cm above tomogram (b)



Fig 9 Normal encephalography. Selected tomograms Lateral ventricles at different levels the foramen of Monro appears in tomogram (b)



Fig 10 Normal temporal bone Selected tomograms a) ossicles at level of aditus, b) lower parts of ossicles at level of mesotympanum 2.0 mm below tomogram (a)

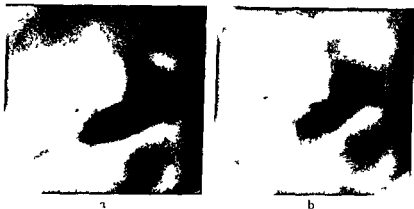


Fig 11 Radical mastoidectomy for cholesteatoma Selected tomograms a) at level of mesotympanum The operation cavity and a defect in the bony wall opening to the posterior fossa are evident b) 2.0 mm above tomogram (a) with the operation defect as well as the loss of the posterior and superior walls of the external auditory meatus as well as that of the ossicles distinguishable

in Fig 11 The transverse tomograms make a complementary analysis of the case possible and reveal a defect in the bony wall, opening to the posterior fossa

*Radiation doses* The exposure dose to the optic lenses and gonads was determined by means of thermoluminescence dosimetry, the dosimeters consisted of LiF teflon plates The dose to the lens is about 0.45 rad per exposure in transverse tomography of the skull base region, this is of the same size as in carotid angiography with the same number of exposures (BERGSTROM et coll 1971) The lens dose in tomography of the ear with a small diaphragm is less than that in carotid angiography by about a tenth The gonad doses are very low and of the same order of magnitude as the background obtained from non-radiated dosimeters

## SUMMARY

A Mimer III tomographic unit equipped with a special device for transverse tomography is described. Technical tests indicate that the system possesses satisfactory functional stability and good resolution. Examples are given of the clinical application of the method.

## ZUSAMMENFASSUNG

Eine tomographische Einheit mit spezieller Zusatzanordnung für transversale Tomographie am Mimer III wird beschrieben. Technische Tests ergeben voll ausreichende Funktionsstabilität des Systems und gutes Auflösungsvermögen. Beispiele illustrieren die klinischen Anwendungsmöglichkeiten.

## RÉSUMÉ

Description d'un appareil tomographique Mimer III équipé d'un dispositif spécial pour la tomographie transverse. Les tests techniques montrent que ce système possède une stabilité fonctionnelle satisfaisante et une bonne résolution. Les auteurs donnent des exemples de l'application clinique de cette méthode.

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## SUPPLEMENTARY PHOTOGRAPHIC TECHNIQUE

### An aid in encephalography

by

JACK I EISENMAN, HENRY F PRIEBRAM and CECILE G JENKIN

A disadvantage in using air to outline the ventricular system is that only portions of the ventricular system can be demonstrated at any one time. In aqueduct stenosis, the length of the affected segment must be determined, as some cases are due merely to a septum (cf Figure). Perforation of such a septum restores normal cerebrospinal fluid circulation (TURNBULL & DRAKE 1966). In the past composite drawings were used to demonstrate the pathology (LASHOLM et coll 1935). With the technique of 'addition' this can be accomplished on one film. This is done in the same manner used to photographically combine the encephalogram and angiogram (ROSEN et coll 1970).

Two films are chosen from an encephalography or a ventriculography. These films must be taken in precisely the same projection and with the same degree of magnification. The only difference is the location of air within the ventricles, cisterns or subarachnoid space.

The equipment is the same as that used in our technique for subtraction (JENKIN et coll 1970). This includes (1) A contact printer using either multi bulb or a single high intensity light controlled by a variable voltage rheostat.



Composite of ventriculogram and encephalogram demonstrating membranous occlusion of the aqueduct

Two and a half to seven and a half cm (1 to 3 inches) below the glass front of the printer is a second glass plate which is used for dodging techniques to modify the resulting contrast of the intermediate and final films. (2) A light meter that has a portable probe used to take intensity reading on different parts of the film (3) A timer to set the duration of light exposure

The film used for the intermediate is a wide contrast scale film. We use Kodak xx super pan, the same film that we use for making the diapositive for the subtraction procedure. This film is available from photographic suppliers.

*Procedure* One of the two films is taped to the glass front of the printer and the second film is laid on top of the first. The rheostat controlled light is turned up to penetrate both films. The films are superimposed exactly by aligning landmarks such as the sella turcica, the frontal and occipital bones. The second film is then taped to the first.

In the same manner as in the first stage of the subtraction technique, a diapositive (reversed copy) is made of the precisely superimposed films. The light intensity is determined by varying the rheostat voltage sufficiently to produce predetermined readings on the lightmeter. This light intensity is used for a constant exposure time. We use three seconds in our routine procedure.

The film is processed in a medium speed automatic processor (Kodak M5), in hand tanks with roentgen developer or in trays with fine grain developer.

The resulting diapositive is now taped to the glass front printer. Light readings are made again to determine the necessary light intensity to make a reversed copy. The copy is printed on conventional roentgen film and processed in the 90 second automatic processor (Kodak M6). For finer detail necessary for publication, DuPont Cronar Commercial S film is used.



### Acknowledgement

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### SUMMARY

A photographic method is described for making a composite image of different films from encephalography. The resultant 'addition' film will enhance the diagnostic and teaching value of the examination.

### ZUSAMMENFASSUNG

Eine photographische Methode, ein zusammengesetztes Bild von verschiedenen Filmen einer Encephalographie herzustellen, wird beschrieben. Der resultierende 'zusätzliche' Film erweitert den diagnostischen und pädagogischen Wert der Untersuchung.

### RÉSUMÉ

Description d'une méthode photographique donnant une image composite de différents films d'une encéphalographie. Le film d'"addition" obtenu augmentera la valeur diagnostique et pédagogique de l'examen.

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## HEAD CLAMP WITH AUTOTOMOGRAPHIC DEVICE FOR PNEUMOGRAPHY

by

VILEN TOLPESHIKOV

Several types of head clamps with autotomographic devices are available for pneumography and may be roughly classified as 'soft' (LINDGREN 1961, NEW 1962, SCHECHTER & STRENGER 1962) and 'rigid' (AMPLATZ 1963). The soft clamps are convenient both for the patient and the examiner and allow the head to be tilted as required without a change in the position of the body. However, these designs do not prevent involuntary movements of the head nor ensure a stable rotation axis during autotomography. Changing the tilt of the head by moving the straps of the clamp and adjusting the fastening require a certain amount of time, which is not always convenient.

Rigid head clamps are advantageous for preventing involuntary head movements and for maintaining the position of the rotation axis during autotomography. A change in the tilt of the head must however necessitate an alteration in the position of the entire body, which complicates the introduction of the gas and the roentgenography.

A head clamp of rigid form has been designed and employed in our department for some time. Involuntary movements of the head are inhibited by two

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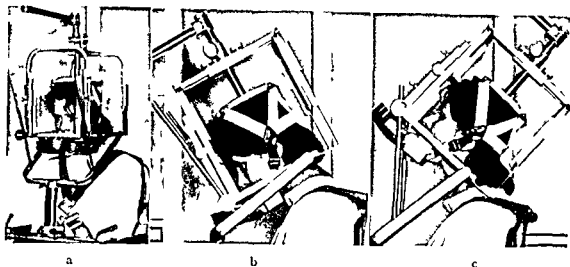


Fig 1 Head clamp for pneumography. General view (a). Forward (b) and backward (c) tilts of the head.

pads arranged according to the ROBERTSON principle (1946). The lower pad, serving as a support for the chin, remains stationary. The upper pad covering the crown may be moved in sagittal and vertical directions, depending on the size and shape of the head, as well as around the vertical axis. The upper pad may be readily locked in any position. The head may be tilted by turning the clamp around horizontal semiaxes located at the level of the atlanto-occipital joint; the degree of tilt possible amounts to  $70^\circ$  (approximately  $50^\circ$  forwards and  $20^\circ$  backwards). The position selected is fixed by means of a single screw. For sideway turns of the head, in particular for autotomography purposes, the BURROWS method (1962) is used, i.e. the head is secured to the upper pad by straps and rotates with it.

Any cassette holder with a mobile grid may be employed for the roentgenography. However, small-sized structures of the posterior cranial fossa and of the base and stem of the brain may be examined by means of a narrow beam of rays without a grid; for this purpose the clamp is furnished with frames (two at the sides and one in the front) holding  $18\text{ cm} \times 24\text{ cm}$  and  $13\text{ cm} \times 18\text{ cm}$  cassettes. The front frame may be angled as required to the central ray. The position of the cassettes with regard to the skull remains fixed irrespective of the head tilt, thus simplifying the roentgenography.

Over a thousand tests carried out with the appliance have confirmed its convenience and reliability, in particular in the examination of mental, unconscious, and other difficult patients.

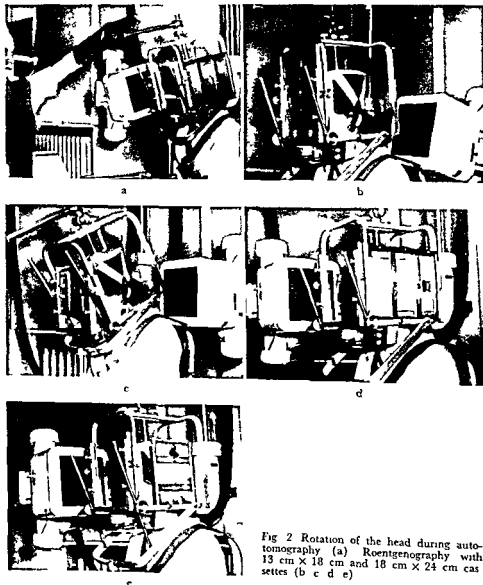


Fig 2 Rotation of the head during autotomography (a) Roentgenography with 13 cm x 18 cm and 18 cm x 24 cm cassettes (b c d e)

### SUMMARY

A head clamp for pneumography is described. This is of solid construction, prevents movement and enables the head to be turned as required.

## ZUSAMMENFASSUNG

Ein Kopfhalter für Pneumographie wird beschrieben. Dieser ist von solidem Bau, verhindert Bewegung und ermöglicht die Drehung des Kopfes in gewünschter Richtung.

## RÉSUMÉ

L'auteur décrit une pince à tête pour la pneumographie. Elle est solide, empêche les mouvements et permet de tourner la tête selon les besoins.

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